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, 2018

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)

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 2, 2018, there were 162,059,718 shares of the registrant's Common Stock outstanding.

INDEX

		Page
	PART I. FINANCIAL INFORMATION	
Item 1.	Financial Statements	3
	Condensed Balance Sheets *as of September 30, 2018 and December 31, 2017*	3
	Condensed Statements of Comprehensive Loss *for the three and nine months ended September 30, 2018 and 2017*	4
	Condensed Statements of Cash Flows *for the nine months ended September 30, 2018 and 2017*	5
	Notes to Condensed Financial Statements	6
Item 2.	Management's Discussion and Analysis of Financial Condition and Results of Operations	19
Item 3.	Quantitative and Qualitative Disclosures about Market Risk	31
Item 4.	Controls and Procedures	31
	PART II. OTHER INFORMATION	
Item 1.	Legal Proceedings	32
Item 1A.	Risk Factors	32
Item 2.	Unregistered Sales of Equity Securities and Use of Proceeds	56
Item 3.	Defaults Upon Senior Securities	56
Item 4.	Mine Safety Disclosures	56
Item 5.	Other Information	56
Item 6.	Exhibits	56
Signatures		57

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

DURECT CORPORATION

CONDENSED BALANCE SHEETS
(in thousands)

	September 30, 2018 (unaudited)	December 31, 2017 (Note 1)
ASSETS		
Current assets:		
Cash and cash equivalents	$ 38,217	$ 29,375
Short-term investments	3,090	7,384
Accounts receivable (net of allowances of $68 at September 30, 2018 and $155 at December 31, 2017)	1,606	2,376
Inventories, net	3,485	3,163
Prepaid expenses and other current assets	2,870	3,060
Total current assets	49,268	45,358
Property and equipment, net	677	929
Goodwill	6,399	6,399
Long-term restricted investments	150	150
Other long-term assets	366	277
Total assets	$ 56,860	$ 53,113
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,152	$ 1,520
Accrued liabilities	5,200	5,511
Contract research liabilities	1,375	834
Deferred revenue, current portion	13	682
Term loan, current portion, net	10,390	7,281
Total current liabilities	18,130	15,828
Deferred revenue, non-current portion	812	1,093
Term loan, non-current portion, net	9,500	12,634
Other long-term liabilities	2,324	2,070
Commitments and contingencies		
Stockholders' equity:		
Common stock	16	15
Additional paid-in capital	487,403	465,246
Accumulated other comprehensive loss	—	(1)
Accumulated deficit	(461,325)	(443,772)
Stockholders' equity	26,094	21,488
Total liabilities and stockholders' equity	$ 56,860	$ 53,113

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

DURECT CORPORATION

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

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Collaborative research and development and other revenue	$ 5,691	$ 5,602	$ 7,432	$ 7,304
Product revenue, net	2,345	2,644	7,505	9,828
Revenue from sale of intellectual property rights	-	12,500	-	12,500
Total revenues	8,036	20,746	14,937	29,632
Operating expenses:				
Cost of product revenues	912	3,105	3,170	5,572
Research and development	6,542	8,378	19,614	25,005
Selling, general and administrative	2,870	3,138	8,880	9,862
Total operating expenses	10,324	14,621	31,664	40,439
Income (Loss) from operations	(2,288)	6,125	(16,727)	(10,807)
Other income (expense):				
Interest and other income	234	605	632	680
Interest expense	(661)	(619)	(1,928)	(1,803)
Net other expense	(427)	(14)	(1,296)	(1,123)
Net income (loss)	$ (2,715)	$ 6,111	$ (18,023)	$ (11,930)
Net change in unrealized loss on available-for-sale securities, net of reclassification adjustments and taxes	-	3	1	3
Total comprehensive income (loss)	$ (2,715)	$ 6,114	$ (18,022)	$ (11,927)
Net income (loss) per share				
Basic	$ (0.02)	$ 0.04	$ (0.11)	$ (0.08)
Diluted	$ (0.02)	$ 0.04	$ (0.11)	$ (0.08)
Weighted-average shares used in computing net income (loss) per share				
Basic	162,002	147,213	159,091	143,873
Diluted	162,002	151,885	159,091	143,873

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,	
	2018	**2017**
Cash flows from operating activities		
Net loss	$ (18,023)	$ (11,930)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Sale of intellectual property rights for non-operating purposes	-	(500)
Depreciation and amortization	162	333
Stock-based compensation	1,839	1,929
Inventory write-down	228	2,176
Amortization of debt issuance cost	80	46
Net amortization (accretion) on investments	70	(61)
Changes in assets and liabilities:		
Accounts receivable	770	(1,026)
Inventories	(547)	(50)
Prepaid expenses and other assets	101	(937)
Accounts payable	(368)	(28)
Accrued and other liabilities	1,975	1,897
Contract research liabilities	541	(55)
Deferred revenue	(479)	14,295
Total adjustments	4,372	18,019
Net cash (used in) provided by operating activities	(13,651)	6,089
Cash flows from investing activities		
Sale of intellectual property rights for non-operating purposes	-	500
Purchases of property and equipment	(73)	(81)
Purchases of available-for-sale securities	(6,893)	(5,248)
Proceeds from maturities of available-for-sale securities	11,118	18,533
Net cash provided by investing activities	4,152	13,704
Cash flows from financing activities		
Payments on equipment financing obligations	(10)	(10)
Payment of additional issuance cost for term loan	(105)	-
Net proceeds from issuances of common stock	18,456	10,100
Net cash provided by financing activities	18,341	10,090
Net increase in Cash, cash equivalents, and restricted cash	8,842	29,883
Cash, cash equivalents, and restricted cash, beginning of the period	29,525	5,554
Cash, cash equivalents, and restricted cash, end of the period (1)	$ 38,367	$ 35,437
Supplementary disclosure of non-cash financing information		
Fully vested options issued to settle accrued liabilities	$ 1,860	$ 1,600

(1) Includes restricted cash of $150,000 (in long term restricted investments) included in the condensed balance sheets at both September 30, 2018 and September 30, 2017.

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 the Company's 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) Drug Delivery 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 products under development by itself and with third party collaborators. The Company also manufactures and sells osmotic pumps used in laboratory research, and designs, develops and manufactures a wide range of standard and custom biodegradable polymers and excipients for pharmaceutical and medical device 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

The accompanying unaudited financial statements include the accounts of the Company. These financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (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 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, 2018, the operating results and comprehensive loss for the three and nine months ended September 30, 2018 and 2017, and cash flows for the nine months ended September 30, 2018 and 2017. The balance sheet as of December 31, 2017 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, 2017 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, 2018, the Company had an accumulated deficit of $461.3 million as well as negative cash flows from operating activities for the nine months ended September 30, 2018.

The Company historically 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. Management's plans in order to meet its operating cash flow requirements include seeking additional collaborative agreements for certain of its programs and achieving milestone and other payments under its collaboration and licensing agreements as well as 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 and that the Company will succeed in its future operations. If the Company cannot successfully raise additional capital and implement its strategic development plan, its liquidity, financial condition and business prospects will be materially and adversely affected.

Inventories

Inventories are stated at the lower of cost or net realizable value, with cost determined on a first-in, first-out basis. Inventories are capitalized based on management's judgment of probable sale prior to their expiration dates. The valuation of inventory requires management to estimate the value of inventory that may become expired prior to use. The Company may be required to expense previously capitalized inventory costs upon a change in management's judgment due to, among other potential factors, a denial or delay of approval of a customer's product by the necessary regulatory bodies, or 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 associated cost of goods for these materials.

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

	September 30, 2018	December 31, 2017
	(unaudited)	
Raw materials	$ 256	$ 282
Work in process	1,540	1,182
Finished goods	1,689	1,699
Total inventories	$ 3,485	$ 3,163

Revenue Recognition

Effective January 1, 2018, the Company adopted FASB ASC Topic 606, Revenue from Contracts with Customers, or ASC 606. In accordance with ASC 606, the Company changed certain characteristics of its revenue recognition accounting policy as described below. ASC 606 was applied using the modified retrospective method, where the cumulative effect of the initial application was recognized as an adjustment to opening retained earnings at January 1, 2018. Therefore, comparative prior periods have not been adjusted and continue to be reported under FASB ASC Topic 605, Revenue Recognition, or ASC 605. The Company recorded a net increase to opening retained earnings of $470,000 with an offset entry to a contra liability account as of January 1, 2018 due to the cumulative impact of adopting Topic 606, with the impact relating to the Company's deferred collaborative research and development revenues. There was no impact to reported total assets, revenues and operating expenses for the three and nine months ended September 30, 2018 as a result of applying Topic 606.

Product Revenue, Net

The Company sells osmotic pumps used in laboratory research, and designs, develops and manufactures a wide range of standard and custom biodegradable polymers and excipients for pharmaceutical and medical device 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: Consistent with industry practice, the Company generally offers customers a limited right of return for products that have been purchased from the Company. The Company estimates the amount of its product sales that may be 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 using its own historical sales information. The Company expects product returns to be minimal.

Collaborative Research and Development Revenues

The Company enters into license agreements which are within the scope of Topic 606, under which it licenses certain rights to its product candidates 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 and commercial milestone payments; payments for manufacturing supply services the Company provides 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 royalty 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. As part

of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company uses key assumptions to determine the stand-alone selling price, which 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 revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes 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 appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

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. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaborative research and development revenues and net income (loss) in the period of adjustment. The Company earned a $5.0 million milestone payment from Indivior UK Limited ("Indivior") upon NDA approval of PERSERIS in the three months ended September 30, 2018.

Manufacturing Supply Services: Arrangements that include a promise for future supply of 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 licensee and if so, they are accounted for as separate performance obligations. If the Company is entitled to additional payments when the customer exercises these options, any additional payments are recorded in collaborative research and development revenue when the customer obtains control of the goods, which is upon delivery.

Royalties and Earn-outs: For arrangements that include sales-based royalties or earn-outs, including milestone payments based on 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 any significant royalty revenue resulting from the Company's collaborative arrangements or any earn-out revenue from the Company's patent purchase agreement with Indivior.

The Company receives payments from its customers based on development cost schedules established in each contract. Up-front payments and fees 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 for the three and nine months ended September 30, 2018 and 2017 are as follows (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
United States	$ 1,931	$ 3,243	$ 6,129	$ 8,609
Europe	5,585	16,812	7,088	18,490
Japan	149	317	722	1,097
Other	371	374	998	1,436
Total	$ 8,036	$ 20,746	$ 14,937	$ 29,632

The cumulative effect of the changes made to the Company's January 1, 2018 balance sheet for the adoption of ASC 606 *Revenue – Revenue from Contract with Customers* was as follows (in thousands):

	Balance at December 31, 2017	Adjustments Due to ASC606	Balance at January 1, 2018
Condensed Balance Sheets			
Liabilities			
Deferred revenue, non-current portion	$ 1,093	$ 470	$ 623
Equity			
Accumulated deficit	$ (443,772)	$ 470	$ (443,302)

During the three and nine months ended September 30, 2018, the Company did not recognize any revenue as a result of changes in the contract asset and the contract liability balances associated with the Company's deferred research and development revenues for the Company's collaboration agreements as a result of adoption of ASC 606.

In accordance with the new revenue standard requirements, the disclosure of the impact of adoption on condensed balance sheets, condensed statements of comprehensive loss, and condensed statements of cash flows for the period ended September 30, 2018 was as follows (in thousands):

	As of September 30, 2018		
	As reported	Balances without adoption of ASC 606	Effect of change Higher/(Lower)
Condensed Balance Sheets			
Liabilities			
Deferred revenue, non-current portion	$ 812	$ 1,282	$ (470)

	For the nine months ended September 30, 2018		
	As reported	Balances without adoption of ASC 606	Effect of change Higher/(Lower)
Condensed Statements of Comprehensive Loss			
Collaborative research and development and other revenue	$ 7,432	$ 7,432	$ -
Product revenue, net	7,505	7,505	-
Total revenues	$ 14,937	$ 14,937	$ -

	For the nine months ended September 30, 2018		
	As reported	Balances without adoption of ASC 606	Effect of change Higher/(Lower)
Condensed Statements of Cash Flow			
Cash flow from Operating Activities			
Deferred revenue, non-current portion	$ (479)	$ -	$ (479)

For the reporting periods before January 1, 2018, revenue was recognized under ASC 605, *Revenue Recognition*. For a detailed description for the Company's revenue recognition policy prior to January 1, 2018, please see Note 1, "Revenue Recognition" to the Company's audited financial statements included in its annual report on Form 10-K for the year ended December 31, 2017.

Comprehensive Income (Loss)

Components of other comprehensive income (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 presented in the Company's Statements of Comprehensive Loss.

Net Income (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,	
	2018	2017	2018	2017
Numerators:				
Net income (loss)	(2,715)	6,111	(18,023)	(11,930)
Denominator:				
Weighted average shares used to compute basic net income (loss) per share	162,002	147,213	159,091	143,873
Dilutive common shares from stock options and ESPP	-	4,672	-	-
Weighted average shares used to compute diluted net income (loss) per share	162,002	151,885	159,091	143,873
Net income (loss) per share:				
Basic	$ (0.02)	$ 0.04	$ (0.11)	$ (0.08)
Diluted	$ (0.02)	$ 0.04	$ (0.11)	$ (0.08)

Options to purchase approximately 17.2 million and 15.6 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, 2018, respectively, as the effect would be anti-dilutive. Options to purchase approximately 20.0 million shares of common stock were excluded from the denominator in the calculation of diluted net loss per share for the nine months ended September 30, 2017, as the effect would be anti-dilutive.

Recently Adopted Accounting Standards

In November 2016, the FASB issued ASU 2016-18, "Statement of Cash Flows (Topic 230): Restricted Cash." The FASB issued the update to clarify how restricted cash or restricted cash equivalents should be presented in the statement of cash flows. The standard will be effective for fiscal years beginning after December 15, 2017, including interim periods within those years, and the guidance will generally be applied retroactively. The Company has adopted the amendments provided in ASU 2016-18 in these condensed financial statements to provide financial statement users with more transparent disclosure about restricted cash and restricted cash equivalents. Upon adoption, the amendments provided in this update are applied using a retrospective transition method to each period presented. The cash, cash equivalents, restricted cash, and restricted cash equivalents balance included $150,000 of restricted cash and restricted cash equivalents as of both September 30, 2018 and December 31, 2017. Restricted cash and restricted cash equivalents are included in long-term restricted investments in the accompanying condensed balance sheets as of September 30, 2018 and December 31, 2017, respectively.

In March 2018, the FASB issued ASU 2018-05, "Income Taxes (Topic 740), Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118." The ASU adds various Securities and Exchange Commission ("SEC") paragraphs pursuant to the issuance of the December 2017 SEC Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act ("SAB 118"), which was effective immediately. The SEC issued SAB 118 to address concerns about reporting entities' ability to timely comply with the accounting requirements to recognize all of the effects of the Tax Cuts and Jobs Act in the period of enactment. SAB 118 allows disclosure that timely determination of some or all of the income tax effects from the Tax Cuts and Jobs Act are incomplete by the due date of the financial statements and if possible to provide a reasonable estimate. The Company has accounted for the tax effects of the Tax Cuts and Jobs Act under the guidance of SAB 118, on a provisional basis. The Company's accounting for certain income tax effects is incomplete, but the Company has determined reasonable estimates for those effects and has recorded provisional amounts in its condensed financial statements as of September 30, 2018 and December 31, 2017.

Recently Issued Accounting Standards

In August 2018, the FASB issued Accounting Standards Update ("ASU") No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement*, which eliminates certain disclosure requirements for fair value measurements for all entities, requires public entities to disclose certain new information and modifies some disclosure requirements. This standard is effective for fiscal years beginning after December 15, 2019, including interim

reporting periods within those years, with early adoption permitted. The Company does not expect the adoption of this standard to have a material effect on its financial statements.

In June 2018, the FASB issued Accounting Standards Update ("ASU") No. 2018-07, *Compensation – Stock Compensation (Topic 718)*, which expands the scope of ASC 718 to include all share-based payment arrangements related to the acquisition of goods and services from both nonemployees and employees. Under the new standard, most of the guidance on stock compensation payments to nonemployees would be aligned with the requirements for share-based payments granted to employees. This standard is effective for fiscal years beginning after December 15, 2018, including interim reporting periods within those years, with early adoption permitted. The Company does not expect the adoption of this standard to have a material effect on its financial statements.

In February 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2018-02, "Income Statement – Reporting Comprehensive Income (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income." The FASB issued the update to provide amended guidance to "allow a reclassification from accumulated other comprehensive income to retained earnings for stranded tax effects resulting from the Tax Cuts and Jobs Act." Additionally, under the new guidance an entity will be required to provide certain disclosures regarding stranded tax effects. The guidance is effective for fiscal years beginning after December 15, 2018, including interim periods within those years, and the guidance may be applied either in the period of adoption or retrospectively to each period (or periods) in which the effect of the change in the U.S. federal income tax rate in the Tax Cuts and Jobs Act is recognized. Early adoption is permitted. The Company does not expect the adoption of this standard to have a material effect on its financial statements.

In February 2016, the FASB issued ASU 2016-02, "Leases (Topic 842)." The FASB issued the update to require the recognition of lease assets and lease liabilities on the balance sheet of lessees. The standard will be effective for fiscal years beginning after December 15, 2018, including interim periods within such fiscal years. The ASU requires a modified retrospective transition method with the option to elect a package of practical expedients. Early adoption is permitted. The Company expects adoption to increase the assets and liabilities recorded on its condensed balance sheet and increase the level of disclosures related to leases. The Company has identified the major leasing arrangements for which transition adjustments will be recorded and the package of practical expedients which will be elected. In addition, the Company anticipates recognition of additional assets and corresponding liabilities related to leases on the Company's Condensed Balance Sheets upon adoption of the ASU.

Note 2. Strategic Agreements

The collaborative research and development and other revenues associated with the Company's major collaborators or counterparties are as follows (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Collaborator/Counterparty				
Indivior UK Limited (Indivior) (1)	$ 5,000	$ -	$ 5,000	$ -
Sandoz AG (Sandoz) (2)	-	3,846	-	4,615
Santen Pharmaceutical Co. Ltd. (Santen) (3)	-	85	1	234
Pain Therapeutics, Inc. (Pain Therapeutics)	-	4	-	109
Zogenix, Inc. (Zogenix) (4)	-	750	-	835
Others (5)	691	917	2,431	1,511
Total collaborative research and development and other revenue	$ 5,691	$ 5,602	$ 7,432	$ 7,304

(1) Amount related to a $5.0 million milestone payment earned in each of the three and nine months ended September 30, 2018, compared to zero for the corresponding periods in 2017.

(2) Amounts related to ratable recognition of upfront fees were zero for each of the three and nine months ended September 30, 2018, compared to $3.8 million and $4.6 million for the corresponding periods in 2017.

(3) Amounts related to ratable recognition of upfront fees were zero for each of the three and nine months ended September 30, 2018, compared to $48,000 and $153,000 for the corresponding periods in 2017.

(4) Amounts related to ratable recognition of upfront fees were zero for each of the three and nine months ended September 30, 2018, compared to $750,000 and $833,000 for the corresponding periods in 2017. In August 2017, the Company and Zogenix terminated their Development and License Agreement dated July 11, 2011 relating to the development and commercialization of Relday.

(5) Includes revenue recognized associated with the Company's feasibility agreements for each of the three and nine months ended September 2018 and 2017.

Agreement with Sandoz AG

In May 2017, the Company and Sandoz AG ("Sandoz") entered into a license agreement to develop and market POSIMIR® (SABER®-bupivacaine) in the United States. Following expiration of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 (HSR), the agreement became effective in June 2017. POSIMIR is the Company's investigational post-operative pain relief depot that utilizes the Company's patented SABER technology to deliver bupivacaine to provide up to three days of pain relief after surgery. The Company retains commercialization rights in the rest of the world. Under terms of the agreement, Sandoz made an upfront payment of $20 million, and the Company remains eligible for up to an additional $30 million in milestone payments based on successful development and regulatory milestones, up to an additional $230 million in sales-based milestones, and a tiered double-digit royalty on product sales for a defined period. DURECT was responsible for the completion of the ongoing PERSIST Phase 3 clinical trial for POSIMIR as well as FDA interactions through potential approval. If approved, DURECT also has certain manufacturing obligations under this agreement. Sandoz will have exclusive commercialization rights in the United States upon regulatory approval with sole funding responsibility for commercialization activities. Sandoz will pay the Company a tiered double-digit royalty on product sales for a defined period, after which the license granted to Sandoz shall convert to a non-exclusive, fully paid, royalty-free, irrevocable and perpetual license. The term of the agreement shall be for the duration of Sandoz's obligation to pay royalties for product sales under the Agreement. The agreement provides each party with specified termination rights, including the right of Sandoz to terminate at will after a specified period and each party to terminate the agreement upon material breach of the agreement by the other party. The failure of the PERSIST trial for POSIMIR to achieve its primary endpoint gives Sandoz a right to terminate the Company's agreement with them on thirty days' notice, in addition to the rights they have to terminate for convenience on six months' notice. In May 2018, the Company and Sandoz entered into an amendment (the "Amendment") to the license agreement. Pursuant to the Amendment, the Company is eligible for up to $30 million in milestone payments based on NDA approval, and remains eligible for up to an additional $230 million in sales-based milestones and a tiered double-digit royalty on product sales for a defined period. Pursuant to the Amendment, each party is also permitted to develop or commercialize competing products. The Amendment also includes modifications to the Company's development obligations and to both parties' termination provisions, including a right for the Company to terminate for convenience prior to NDA approval, and a new termination fee payable to the Company in the event that Sandoz terminates the agreement for convenience. Except as expressly set forth in the Amendment, the license agreement remains in full force and effect.

The Company evaluated the agreement under the accounting guidance for multiple element arrangements and identified three deliverables: the license to develop and market POSIMIR, the research and development services and the manufacturing services. Given that the delivery of the manufacturing services by the Company is dependent upon approval of POSIMIR by the FDA, and that the fee to be received by the Company for these services, should they be delivered, is consistent with their estimated selling price, the Company considers the manufacturing services to be a contingent deliverable and has excluded them from the initial measurement and allocation of the arrangement consideration. The Company evaluated the license deliverable and concluded that it did not have stand alone value separate from the research and development services and accordingly combined these deliverables into a single unit of accounting. The Company allocated the arrangement consideration, which consists of the $20.0 million upfront payment, to this single unit of accounting. As of December 31, 2017, all of the $20.0 million upfront fee had been recognized as revenue as the Company's contractual performance obligations had been fulfilled.

Total collaborative research and development revenue recognized by the Company for Sandoz was zero for each of the three and nine months ended September 30, 2018, compared with $3.8 million and $4.6 million for the corresponding periods in 2017. The cumulative aggregate payments received by the Company from Sandoz as of September 30, 2018 were $20.0 million under this agreement.

Patent Purchase Agreement with Indivior

On September 26, 2017, the Company entered into a Patent Purchase Agreement (the "Agreement") with Indivior. Pursuant to the Agreement, the Company has assigned to Indivior certain patents that may provide further intellectual property protection for PERSERIS™ (risperidone), Indivior's extended-release injectable suspension for the treatment of schizophrenia in adults. In consideration for such assignment, Indivior made an upfront non-refundable payment to DURECT of $12.5 million. Indivior also agreed to make an additional $5.0 million payment to DURECT contingent upon NDA approval of PERSERIS, as well as quarterly earn-out payments that are based on a single digit percentage of U.S. net sales for certain products covered by the assigned patent rights, including PERSERIS. The assigned patent rights include granted patents extending through at least 2026. DURECT also receives a non-exclusive right under the assigned patents to develop and commercialize certain risperidone-containing products and products that do not contain risperidone or buprenorphine. The agreement contains customary representations, warranties and indemnities of the parties. The Company received the payment of $12.5 million from Indivior in September 2017 and recognized the $12.5 million as revenue from sale of intellectual property rights in 2017 as the Company did not have any continuing obligations under the purchase agreement. On July 27, 2018, Indivior announced that the FDA had approved the NDA for PERSERIS thereby triggering the $5.0 million payment to DURECT; this payment was received by DURECT in August 2018. The Company recognized

the $5.0 million as milestone revenue during the three months ended September 30, 2018 as there is no further performance obligation associated with this milestone payment.

Agreement with Pain Therapeutics, Inc.

In December 2002, the Company entered into an exclusive agreement with Pain Therapeutics, Inc. (Pain Therapeutics) to develop and commercialize on a worldwide basis REMOXY ER and other oral sustained release, abuse deterrent opioid products incorporating four specified opioid drugs, using the ORADUR technology. This agreement currently covers only REMOXY ER.

Under the terms of this agreement, Pain Therapeutics paid the Company an upfront license fee of $1.0 million, with the potential for an additional $3.0 million in performance milestone payments based on the successful development and approval of REMOXY ER. Of these potential milestones, all $3.0 million are development-based milestones. There are no sales-based milestones under the agreement. As of September 30, 2018, the Company had received $1.5 million in cumulative milestone payments.

Following multiple Complete Response Letters, in February 2018, Pain Therapeutics stated that they had resubmitted the REMOXY ER NDA. On August 6, 2018, Pain Therapeutics stated that it had received a Complete Response Letter from the FDA, which concluded that "The data submitted in [the] NDA do not support the conclusion that the benefits of [REMOXY] Extended-Release Capsules outweigh the risks." Pain Therapeutics further announced a strategic reorganization to align its resources on advancing its drug and diagnostic assets in Alzheimer's disease.

Total collaborative research and development revenue recognized for REMOXY-related work performed by the Company for Pain Therapeutics was zero for each of the three and nine months ended September 30, 2018, respectively, compared with $4,000 and $109,000 for the corresponding periods in 2017. The cumulative aggregate payments received by the Company from Pain Therapeutics as of September 30, 2018 were $40.4 million under this agreement.

Agreement with Zogenix, Inc.

On July 11, 2011, the Company and Zogenix, Inc. (Zogenix) entered into a Development and License Agreement (the Zogenix Agreement). The Company and Zogenix had previously been working together under a feasibility agreement pursuant to which the Company's research and development costs were reimbursed by Zogenix. Under the Zogenix Agreement, Zogenix was responsible for the clinical development and commercialization of a proprietary, long-acting injectable formulation of risperidone using the Company's SABER controlled-release formulation technology potentially in combination with Zogenix's DosePro® needle-free, subcutaneous drug delivery system. DURECT was responsible for non-clinical, formulation and CMC development activities. The Company was to be reimbursed by Zogenix for its research and development efforts on the product. Zogenix paid a non-refundable upfront fee to the Company of $2.25 million in July 2011. The Company's research and development services were considered integral to utilizing the licensed intellectual property and, accordingly, the deliverable was accounted for as a single unit of accounting. The $2.25 million upfront fee had been recognized as collaborative research and development revenue ratably over the term of the Company's research and development involvement with Zogenix with respect to this product candidate.

The Company granted to Zogenix an exclusive worldwide license, with sub-license rights, to the Company's intellectual property rights related to the Company's proprietary polymeric and non-polymeric controlled-release formulation technology to make and have made, use, offer for sale, sell and import risperidone products, where risperidone is the sole active agent, for administration by injection in the treatment of schizophrenia, bipolar disorder or other psychiatric related disorders in humans. The Company retained the right to supply Zogenix's Phase 3 clinical trial and commercial product requirements on the terms set forth in the Zogenix Agreement. Zogenix was permitted to terminate the Zogenix Agreement without cause at any time upon prior written notice, and either party was permitted to terminate the Zogenix Agreement upon certain circumstances including written notice of a material uncured breach.

In August 2017, the Company and Zogenix terminated the Zogenix Agreement. Under the mutual termination agreement, Zogenix's development and commercialization rights were returned to the Company, and Zogenix has transferred to the Company all regulatory filings and development information related to Relday. As a result of the termination of the Zogenix agreement, the Company recognized revenue during the third quarter of 2017 for the remaining $750,000 of deferred revenue related to the upfront fee as the Company had no remaining performance obligations under the agreement; this recognition of revenue did not result in additional cash proceeds to the Company.

Agreement with Santen Pharmaceutical Co., Ltd.

On December 11, 2014, the Company and Santen Pharmaceutical Co., Ltd. (Santen) entered into a definitive agreement (the Santen Agreement). Pursuant to the Santen Agreement, the Company granted Santen an exclusive worldwide license to the Company's proprietary SABER formulation platform and other intellectual property to develop and commercialize a sustained release product utilizing the Company's SABER technology to deliver an ophthalmology drug. Santen controls and funds the development

and commercialization program, and the parties established a joint management committee to oversee, review and coordinate the development activities of the parties under the Santen Agreement.

In connection with the Santen agreement, Santen agreed to pay the Company an upfront fee of $2.0 million in cash and to make contingent cash payments to the Company of up to $76.0 million upon the achievement of certain milestones, of which $13.0 million are development-based milestones and $63.0 million are commercialization-based milestones including milestones requiring the achievement of certain product sales targets (none of which has been achieved as of September 30, 2018). Santen will also pay for certain Company costs incurred in the development of the licensed product. If the product is commercialized, the Company would also receive a tiered royalty on annual net product sales ranging from single-digit to the low double digits, determined on a country-by-country basis. As of September 30, 2018, the cumulative aggregate payments received by the Company under this agreement were $3.3 million.

The following table provides a summary of collaborative research and development revenue recognized under the Santen Agreement (in thousands).

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Ratable recognition of upfront payment	$ -	$ 48	$ -	$ 153
Research and development expenses reimbursable by Santen	-	37	1	81
Total collaborative research and development revenue	$ -	$ 85	$ 1	$ 234

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, 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, 2018 is less than twelve months and these investments are rated by S&P and Moody's at AAA or AA- for securities and A1 or P1 for commercial paper.

The following is a summary of available-for-sale securities as of September 30, 2018 and December 31, 2017 (in thousands):

	September 30, 2018			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$ 72	$ -	$ -	$ 72
Certificates of deposit	150	-	-	150
Commercial paper	40,308	-	-	40,308
	$ 40,530	$ -	$ -	$ 40,530
Reported as:				
Cash and cash equivalents	$ 37,290	$ -	$ -	$ 37,290
Short-term investments	3,090	-	-	3,090
Long-term restricted investments	150	-	-	150
	$ 40,530	$ -	$ -	$ 40,530

	December 31, 2017			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Estimated Fair Value
Money market funds	$ 568	$ -	$ -	$ 568
Certificates of deposit	150	-	-	150
Commercial paper	33,307	-	-	33,307
Corporate debt	1,298	-	(1)	1,297
	$ 35,323	$ -	$ (1)	$ 35,322
Reported as:				
Cash and cash equivalents	$ 27,788	$ -	$ -	$ 27,788
Short-term investments	7,385	-	(1)	7,384
Long-term restricted investments	150	-	-	150
	$ 35,323	$ -	$ (1)	$ 35,322

The following is a summary of the cost and estimated fair value of available-for-sale securities at September 30, 2018, by contractual maturity (in thousands):

	September 30, 2018	
	Amortized Cost	Estimated Fair Value
Mature in one year or less	$ 40,458	$ 40,458
	$ 40,458	$ 40,458

There were no securities that have had an unrealized loss for more than 12 months as of September 30, 2018.

As of September 30, 2018, 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. Stock-Based Compensation

As of September 30, 2018, the Company has three 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,	
	2018	2017	2018	2017
Cost of product revenues	$ 24	$ 27	$ 72	$ 83
Research and development	238	374	929	1,057
Selling, general and administrative	277	301	838	789
Total stock-based compensation	$ 539	$ 702	$ 1,839	$ 1,929

As of September 30, 2018 and December 31, 2017, $14,000 of stock-based compensation cost was capitalized in inventory on the Company's balance sheets.

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, 2018 and 2017:

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Stock Options				
Risk-free rate	2.8-3.1%	2.0-2.3%	2.7-3.1%	2.0-2.5%
Expected dividend yield	—	—	—	—
Expected life of option (in years)	9.0-10.0	6.8-10.0	7.0-10.0	6.8-10.0
Volatility	79-85%	75-81%	79-86%	75-82%

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Employee Stock Purchase Plan				
Risk-free rate	2.1%	1.0%	1.3-2.1%	0.6-1.0%
Expected dividend yield	—	—	—	—
Expected life of option (in years)	0.5	0.5	0.5	0.5
Volatility	66%	44%	66-146%	44-81%

Note 5. Term Loan

In July 2016, the Company entered a $20.0 million secured single-draw term loan with Oxford Finance LLC (Oxford Finance). The 2016 Loan Agreement provides 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 the term loan of August 1, 2020. The 2016 Loan Agreement also provides for a floating interest rate (7.95% initially and 9.57% as of September 30, 2018) based on an index rate plus a spread, a $150,000 facility fee that was paid at closing and an additional payment equal to 9.25% of the principal amount of the term loan, which 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 between 1% and 3% of the principal amount of the term loan depending on the timing of prepayment. The facility fee and other debt offering/issuance costs have been recorded as debt discount on the Company's balance sheet and together with the final $1.9 million payment are being amortized to interest expense during the life of the term loan using the effective interest rate method.

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 2016 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 2016 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 2016 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 2016 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.

In February 2018, the Company and Oxford Finance entered into a First Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from March 1, 2018 to December 1, 2018 and to increase the additional payment due when the term loan becomes due or upon the prepayment of the facility from 9.25% of the principal amount of the term loan to 10% of such amount. The interest rate and the maturity date remain unchanged, and the Company paid Oxford Finance a loan modification fee of $100,000.

The fair value of the term loan approximates the carrying value. Future maturities and interest payments due under the term loan as of September 30, 2018, are as follows (in thousands):

Three months ended December 31, 2018	$ 2,305
2019	12,463
2020	8,845
Total minimum payments	23,613
Less amount representing interest	(3,613)
Gross balance of term loan	20,000
Less unamortized debt discount	(110)
Carrying value of term loan	19,890
Less term loan, current portion, net	(10,390)
Term loan, non-current portion, net	$ 9,500

As of September 30, 2018, the Company was in compliance with all material covenants under the Loan Agreement and there had been no material adverse change.

Note 6. Commitments

Operating Leases

In August 2018 and September 2018, the Company entered into lease amendments on a 30,149 square foot facility and a 20,100 square foot facility in Cupertino, California. Both of the leases expire in February 2024 with one option to renew for an additional five years.

The Company has lease arrangements for its facilities in California and Alabama 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
Birmingham, AL	21,540 sq. ft.	Office, Laboratory and Manufacturing	Lease expires 2021 (with two options to renew the lease term for an additional five years each after the current lease expires)

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. Rent expense under all operating leases was $475,000 and $1.4 million for the three and nine months ended September 30, 2018, compared to $464,000 and $1.4 million for the corresponding periods in 2017.

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

	Operating Leases
Three months ended December 31, 2018	$ 491
2019	2,122
2020	2,200
2021	2,126
2022	1,991
Thereafter	2,245
	$ 11,175

Note 7. Stockholders' Equity

During the nine months ended September 30, 2018, the Company raised net proceeds (net of commissions) of approximately $16.8 million from the sale of 9,629,426 shares of the Company's common stock in the open market at a weighted average price of $1.80 per share, through its Controlled Equity Offering sales agreement with Cantor Fitzgerald, entered into in November 2015 (Controlled Equity Offering).

Note 8. Subsequent Events

In November 2015, the Company filed a shelf registration statement on Form S-3 with the SEC, which upon being declared effective in November 2015, allowed the Company to offer up to $125.0 million of securities from time to time in one or more public offerings, inclusive of $40.0 million of common stock which the Company was permitted to sell pursuant to a Controlled Equity Offering sales agreement (the "2015 Sales Agreement") entered into in November 2015 with Cantor Fitzgerald & Co. ("Cantor Fitzgerald"), acting as agent. As of September 30, 2018, approximately 24.6 million shares of common stock were sold through the 2015 Sales Agreement for an aggregate purchase price of approximately $39.5 million. In August 2018, the Company filed a new shelf registration statement on Form S-3 with the SEC, which upon being declared effective in October 2018, terminated the November 2015 registration statement and 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 additional shares of common stock which the Company may sell, subject to certain limitations, under the 2015 Sales Agreement through Cantor Fitzgerald, acting as agent.

On November 1, 2018, the Company and Oxford Finance entered into a Second Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from December 1, 2018 to June 1, 2020 and the final maturity date from August 1, 2020 to November 1, 2022. 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 interest rate and the final payment remain unchanged, and the Company paid Oxford Finance a Second Amendment fee of $900,000.

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, 2018 and 2017 should be read in conjunction with our annual report on Form 10-K for the year ended December 31, 2017 filed with the Securities and Exchange Commission and "Risk Factors" section included elsewhere in this Form 10-Q. 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 report, 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, for example, statements about:

- the clinical trial plans for DUR-928;
- potential regulatory filings for or approval of DUR-928, POSIMIR, REMOXY ER, or any of our or any third parties' other product candidates;
- the potential product launch of PERSERIS by Indivior and the associated earn-out payments we may receive from Indivior;
- the progress of our third-party collaborations, including estimated milestones;
- our intention to seek, and ability to enter into and maintain strategic alliances and collaborations;
- the potential benefits and uses of our products;
- 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 continued development of our products;
- our responsibilities to our third-party collaborators, including our responsibilities to conduct research and development, clinical trials and manufacture products;
- our ability to protect intellectual property, including intellectual property licensed to our collaborators;
- market opportunities for products in our product pipeline;
- the progress and results of our research and development programs and our evaluation of additional development programs;
- requirements for us to purchase supplies and raw materials from third parties, and the ability of third parties to provide us with required supplies and raw materials;
- the results and timing of clinical trials, including for DUR-928 and POSIMIR, the possible commencement of future clinical trials and announcements of the findings of our clinical trials;
- conditions for obtaining regulatory approval of our product candidates;
- submission and timing of applications for regulatory approval;
- the impact of FDA, DEA, EMEA and other government regulation on our business;
- the impact of potential Risk Evaluation and Mitigation Strategies (REMS) on our business;
- uncertainties associated with obtaining, asserting and protecting patents and other intellectual property rights, as well as avoiding the intellectual property rights of others;
- products and companies that will compete with the products we 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 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 for additional financing, including potential sales under our shelf registration statement;
- our expectations regarding marketing expenses, research and development expenses, and selling, general and administrative expenses;
- the composition of future revenues; and
- accounting policies and estimates, including revenue recognition policies.

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.

Overview

We are a biopharmaceutical company with research and development programs broadly falling into two categories: (i) new chemical entities derived from our Epigenetic Regulator Program, in which we attempt to discover and develop molecules which have not previously been approved and marketed as therapeutics, and (ii) Drug Delivery Programs, in which we apply our formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which we aim to improve in some manner through a new formulation. We also manufacture and sell osmotic pumps used in laboratory research and design, develop and manufacture a wide range of standard and custom biodegradable polymers and excipients for pharmaceutical and medical device clients for use as raw materials in their products. In addition, we conduct research and development of pharmaceutical products in collaboration with third party pharmaceutical and biotechnology companies.

A central aspect of our business strategy involves advancing multiple product candidates at one time, which is enabled by leveraging our resources with those of corporate collaborators. Thus, certain of our programs are currently licensed to 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 a royalty on product sales. At the same time, we have retained the rights to other programs, which are the basis of future potential collaborations and which over time may provide a pathway for us to develop our own biopharmaceutical commercial, sales and marketing organization.

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, 2017 and in Note 2 of the financial statements included in Item 1 above.

Epigenetic Regulator Program and New Chemical Entities

DURECT's 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 discoveries from this program are a result of more than 20 years of lipid research by Shunlin Ren, M.D., Ph.D., Professor of Internal Medicine at the VCU Medical Center and a recipient of multiple grants from the National Institutes of Health (NIH) for metabolic disease research. Epigenetic regulation does not change DNA sequences, but regulates the pattern of DNA expression and subsequent cellular functions. DUR-928 is our program's lead product candidate. We hold the exclusive royalty-bearing worldwide right to develop and commercialize DUR-928 and related molecules discovered in the program.

NOTE: POSIMIR®, SABER®, CLOUD®, TRANSDUR®, ORADUR®, ALZET® and LACTEL® are trademarks of DURECT Corporation. Other trademarks referred to belong to their respective owners.

During the course of this program, a number of compounds have been identified that may have therapeutic utility for various uncommon (orphan and rare) and common diseases, disorders or syndromes. The lead compound from this program (DUR-928) is an endogenous, orally available small molecule that modulates the activity of various nuclear receptors that play important regulatory roles in lipid homeostasis, inflammation and cell survival.

The biological activity of DUR-928 has been demonstrated in over 10 different animal disease models involving three animal species. Several of these disease models represent chronic metabolic disorders of hepatic lipid accumulation and dysfunction (e.g., nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH)) and several represent acute organ injuries (endotoxin shock, ischemic-reperfusion kidney injury, acute liver failure and stroke).

We are pursuing the development of DUR-928 through three programs for: (i) chronic metabolic disorders or liver diseases using oral administration, (ii) acute organ injury by injection or infusion, and (iii) local skin inflammatory disorders using topical application. We are also evaluating additional indications beyond these programs.

In pharmacokinetic and/or toxicity studies conducted in mice, hamsters, rats, rabbits, dogs, minipigs and monkeys, DUR-928 has been found to be orally available, locally tolerable and safe by all routes tested to date. These non-clinical results supported the initiation of DUR-928 into human safety/pharmacokinetics (PK)/proof-of-concept trials.

Chronic Metabolic Disease Program with Orally Administered DUR-928

Market Opportunity. Non-alcoholic fatty liver disease (NAFLD) affects approximately 30% of adults and 10% of children (about 81 million individuals) in the United States. There are many mechanisms, but only one phenotype of steatohepatitis. 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 more than 10% of adults in the United States, Europe, Japan and other developed countries. No drug is currently approved for treatment of NAFLD or NASH. Moreover, alcoholic fatty liver disease (AFLD), including its more advanced stage, alcoholic steatohepatitis (ASH), develops in approximately 90% of individuals who drink more than 60 grams/day of alcohol, but may occur in individuals who drink less, and is a major contributor to the global burden of liver cirrhosis. In addition to these liver diseases, there are a number of orphan liver diseases for which we may seek to develop DUR-928.

Clinical Program. The initial Phase 1 trial of DUR-928 was a single-site, randomized, double-blinded, placebo-controlled, single-ascending-dose study that evaluated the safety, tolerability and PK of orally administered DUR-928. The 30-subject study evaluated DUR-928 in five cohorts of healthy volunteers receiving DUR-928 (n=20 on drug, 10 on placebo) at escalating doses that resulted in peak plasma concentrations greater than 100-fold higher than endogenous levels. DUR-928 was well-tolerated at all dose levels, with no serious treatment-related adverse events reported. Dose related increases in plasma concentrations were observed with peak plasma concentration at approximately 2-6 hours after dosing. We subsequently conducted a Phase 1 multiple-ascending-dose, randomized, double-blinded, placebo-controlled, oral administration trial in 20 healthy subjects (n=16 on drug, 4 on placebo). Following multiple dosing, DUR-928 was well-tolerated at all doses, with no serious drug-related adverse events reported and no accumulation in plasma concentrations observed with repeat dosing. We also conducted a food effect study with 8 healthy volunteers and observed no food effect on absorption.

Our first patient trial utilizing orally administered DUR-928 was an open-label, single-ascending-dose safety and PK Phase 1b trial in liver function impaired (NASH) patients and matched control subjects (MCS) (matched by age, body mass index and gender with normal liver function). This study was conducted in Australia in two successive dose cohorts (first a low dose of 50 mg and then a high dose of 200 mg) and NASH patients were confirmed to be either cirrhotic or non-cirrhotic. Both cohorts consisted of 10 NASH patients and 6 MCS. Data from this study was presented at the International Liver Congress™ 2017 organized by the European Association for the Study of the Liver (EASL) in Amsterdam on April 22, 2017.

All patients and MCS tolerated DUR-928 well. One patient (with a prior history of arrhythmia and an ongoing viral infection) in the high dose cohort experienced a serious adverse event (shortness of breath), which occurred without unusually abnormal biochemical changes and resolved without intervention but was considered possibly treatment related by the physician due to its temporal association with dosing. In both the 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 DUR-928 was dose dependent.

While this study was not designed to assess efficacy, we observed a reduction of certain biomarkers after a single oral dose of DUR-928. Exploratory biomarker analysis indicated that a single oral dose of DUR-928 resulted in statistically significant reductions from baseline in the levels of both full-length and cleaved cytokeratin-18 (CK-18), bilirubin, high sensitivity C-Reactive Protein (hsCRP) and IL-18 in the NASH patients. The mean decrease 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 in total bilirubin (a liver function impairment 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 hsCRP, a marker of inflammation, at the measured time point of greatest effect (24 hours after dosing) was 8% on average in the low dose cohort and 13% in the high dose cohort. The mean decrease of IL-18, an inflammatory mediator implicated in both liver and kidney diseases, 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.

Collectively, the reduction of these biomarkers plus results from our animal and cell culture studies suggest potential therapeutic activity of DUR-928 for patients with liver diseases. However, additional studies are required to evaluate the safety and efficacy of DUR-928, and there is no assurance that these biomarker effects will be associated with clinically relevant benefits, or that DUR-928 will demonstrate safety or efficacy in treating liver diseases in larger controlled trials.

We are conducting a Phase 2a trial in PSC with orally administered DUR-928. The Phase 2a trial is a randomized, open label study with two cohorts (a cohort of 10 mg and a cohort of 50 mg), in which patients (n = 15-20 per cohort) receive oral dosing of DUR-928 for four weeks with follow-up for an additional four weeks. The objectives of this study include safety, PK and pharmacodynamic (PD) markers, including the percent change from baseline of serum alkaline phosphatase (ALP) and other biomarkers. To date, five PSC patients have been dosed, and the Company is not able to provide meaningful interim data at this time. The Company plans to continue enrolling patients and will provide an update when enrollment has reached a critical mass for data analysis. PSC is a chronic liver disease characterized by a progression of cholestasis (decrease in bile flow) with inflammation and fibrosis of bile ducts. Over time, PSC leads to liver failure, infections and tumors of the bile duct or liver, and ultimately may require a liver transplant. There is no approved treatment for PSC at this time. We have received orphan drug designation for DUR-928 to treat patients with PSC.

Acute Organ Injury Program with Injectable DUR-928

Market Opportunity. Acute organ injury is another area of major unmet medical need for which effective pharmaceutical treatment is often lacking. Alcoholic liver disease (ALD) is a syndrome characterized by progressive inflammatory liver injury associated with long-term heavy intake of alcohol, and involves a spectrum that ranges from mild injury to severe, life threatening injury. Alcoholic hepatitis (AH), is an acute, inflammatory form of ALD for which there are no effective therapeutics available. The prevalence of AH is believed to be 10-35% of heavy drinkers. There were over 320,000 hospitalizations related to alcoholic hepatitis in 2010, and the hospitalization costs amounted to nearly $50,000 per patient. Acute kidney injury (AKI), a sudden loss of kidney function due to renal failure or injury, affects approximately 2.8 million patients per year in the United States and is associated with increased mortality, prolonged hospital stays, kidney dialysis and progression to chronic kidney disease. There are various forms of acute organ injury affecting the liver, the kidney or other organs for which we may seek to develop DUR-928.

Clinical Program. The initial Phase 1 trial with injectable administration was a single-site, randomized, double-blinded, placebo-controlled, single-ascending-dose study that evaluated the safety, tolerability and PK of intramuscular (IM) injected DUR-928. The 24-subject study (16 healthy volunteers on the drug and 8 on placebo) of four escalating dose levels resulted in dose proportionality of systemic exposure. DUR-928 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 volunteers, in which participants received IM-injected DUR-928 for 5 consecutive days (8 subjects on the drug, 2 on placebo) with the next to highest dose in 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 infusion (IV) study with 16 healthy volunteers and observed no treatment related serious adverse events. The systemic exposure following IV infusion was dose proportional.

We have also completed a Phase 1 drug-drug interaction study. The results demonstrated that neither orally administered nor intravenously injected DUR-928 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.

Our second Phase 1b study with injected DUR-928, also conducted in Australia, was an open-label, single-ascending-dose study in patients with impaired kidney function (stage 3 and 4 chronic kidney disease (CKD)) and matched control subjects (matched by age, body mass and gender with normal kidney function). This study was conducted in two successive cohorts (first a low dose of 30 mg and then a high dose of 120 mg) evaluating safety and PK of single-dose intramuscular injected DUR-928. The low dose cohort consisted of 6 patients with chronic kidney disease and 3 matched control subjects; the high dose cohort consisted of 5 patients with chronic kidney disease and 3 matched control subjects. In this trial, DUR-928 was well tolerated among all subjects and the PK parameters between the kidney function impaired patients and the matched control subjects were comparable. While the number of

subjects involved was small and not designed to assess efficacy, we did observe decreases in bilirubin and CK-18 when those levels were meaningfully elevated pre-treatment, although these results were not statistically significant.

We are conducting a Phase 2a clinical trial with intravenously administered DUR-928 in patients with AH. This is an open label, dose escalation, multi-center U.S. study, originally designed to be conducted in two sequential parts. Part A includes patients with moderate AH (as determined by the Model of End-Stage Liver Disease (MELD) scores, a common scoring system to assess the severity and prognosis of AH patients), and Part B includes patients with severe AH. Three dose levels (30, 90 and 150 mg) are planned for testing in Part A. Dose escalation occurs following review of safety and pharmacokinetic (PK) results of the prior dose level by a Dose Escalation Committee (DEC). The target number of patients for the study is 4-6 per dose group. The objectives of this study include safety, PK and pharmacodynamic (PD) signals, including liver biochemistry and biomarkers. We recently completed dosing for the low-dose 30 mg cohort (n=4) of Part A (moderate AH patients). After completing the safety and PK review by the DEC, DURECT plans to commence the 90 mg cohort in Part A. We have amended the protocol so that after the DEC completes its review, DURECT can begin enrolling Part B (severe AH patients), starting with the low dose, while it simultaneously continues enrolling Part A (moderate AH patients). We believe enrolling Part A and B simultaneously will accelerate the overall timeline for the trial. Over the course of the trial, the clinical sites have encountered many severe AH patients who may have qualified for Part B but were deemed screen failures due to their MELD scores being too high for Part A.

Skin Inflammatory Disorder Program with Topical DUR-928

Market opportunity. Skin inflammatory disorders, such as psoriasis or atopic dermatitis, affect approximately 7.5 million and 32 million Americans, respectively. Most currently available topical treatments, typically as first line therapy, either slow down excessive skin cell proliferation or reduce inflammation. Steroids are the most commonly used topical anti-inflammatory agents because they reduce the swelling and redness of lesions.

Clinical program. We have conducted an exploratory Phase 1b trial in psoriasis patients (9 evaluable patients) in Australia. The double-blinded and placebo-controlled trial was conducted using a micro-plaque assay with intralesional injections of DUR-928. We feel that the initial results were encouraging and warrant further investigation. As a result, we are planning to conduct a Phase 2a proof-of-concept trial with topical DUR-928 in patients with mild to moderate plaque psoriasis beginning in the first quarter of 2019. This will be a multicenter, randomized, double-blind, vehicle-controlled clinical trial conducted in the U.S. Approximately 20 subjects will be enrolled to obtain about 15 evaluable subjects in the study. DUR-928 will be applied topically once-daily for four weeks. Patients will serve as their own controls, as each patient will have similar contralateral plaques. DUR-928 will be applied to one plaque and the vehicle control will be applied to the contralateral plaque daily for four weeks. Patients will be followed for an additional four weeks and the primary efficacy endpoint will be improvement in local psoriasis scores in the DUR-928-treated plaque compared to the vehicle-treated plaque.

POSIMIR® (Extended Release Bupivacaine)

Our post-operative pain relief depot, POSIMIR, is a sustained release injectable using our SABER® delivery system to deliver bupivacaine, an off-patent pharmaceutical agent. SABER is a controlled drug delivery technology that is administered via the parenteral (i.e., injectable) route to deliver drugs that act systemically or locally. POSIMIR is designed to be administered to a surgical site at the end of surgery for post-operative pain relief and is intended to provide local analgesia for up to 3 days, which we believe coincides with the time period of the greatest need for post-surgical pain control in most patients. In May 2017, we signed an agreement with Sandoz whereby Sandoz will have the exclusive commercialization rights to POSIMIR in the United States. DURECT retains the development and commercialization rights to POSIMIR in all other countries. Closing of this transaction occurred in June 2017 upon the expiration of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976. In May 2018, the agreement with Sandoz was amended. Pursuant to the amendment, we are eligible for up to $30 million in milestone payments based on NDA approval, and remain eligible for up to an additional $230 million in sales-based milestones and a tiered double-digit royalty on product sales for a defined period. Pursuant to the amendment, each party is also permitted to develop or commercialize competing products. The amendment also includes modifications to our development obligations and to both parties' termination provisions, including a right for us to terminate for convenience prior to NDA approval, and a new termination fee payable to us in the event that Sandoz terminates the agreement for convenience. Except as expressly set forth in the amendment, the license agreement remains in full force and effect.

In April 2013, we submitted an NDA as a 505(b)(2) application, which relied in part on the FDA's findings of safety and effectiveness of a reference drug. In February 2014, we received a Complete Response Letter from the FDA. Based on the Complete Response Letter and subsequent communications with the FDA, we conducted a new POSIMIR Phase 3 clinical trial (the PERSIST trial) consisting of patients undergoing laparoscopic cholecystectomy (gallbladder removal) surgery to further evaluate the benefits and risks of POSIMIR. We began recruiting patients for this trial in November 2015 comparing POSIMIR to placebo. Based on advice from the FDA received subsequent to the start of the trial, in April 2016 we decided to amend the PERSIST trial. Starting in August 2016, we began implementing Part 2 of the PERSIST trial to evaluate POSIMIR against standard bupivacaine HCl rather than placebo

as we had been doing initially in the study. In October 2017, we reported that the PERSIST trial did not meet its primary efficacy endpoint of reduction in pain on movement over the first 48 hours after surgery as compared to standard bupivacaine HCl. While results trended in favor of POSIMIR versus the comparator, they did not achieve statistical significance. We continue to evaluate and consider potential next steps with the program.

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 an upfront non-refundable payment to DURECT of $12.5 million. Indivior also agreed to make an additional $5 million payment to DURECT contingent upon FDA approval of PERSERIS, as well as quarterly earn-out payments that are based on a single digit percentage of U.S. net sales for certain products covered by the assigned patent rights, including PERSERIS; FDA approval occurred in July 2018 and the $5.0 million milestone payment was received in August 2018. On November 1, 2018, Indivior stated that they are preparing a full promotional launch of PERSERIS with a field force of 40 to 60 representatives, contingent upon the preliminary injunction against Dr. Reddy's Laboratories being upheld by the U.S. Court of Appeals for the Federal Circuit. Indivior further stated that they will be making PERSERIS available in the U.S. in Q4 2018 to begin generating product awareness and trial.

REMOXY® ER

In December 2002, we entered into an agreement with Pain Therapeutics, amended in December 2005, under which we granted Pain Therapeutics the exclusive, worldwide right to develop and commercialize selected long-acting oral opioid products using our ORADUR technology incorporating four specified opioid drugs. This agreement currently covers only REMOXY ER. REMOXY ER, a novel long-acting oral formulation of the opioid oxycodone targeted to decrease the potential for oxycodone abuse, was developed under this agreement. Even where abuse deterrent properties exist, opioid drugs such as oxycodone still expose users to the risks of addiction, abuse and misuse. REMOXY ER is intended for patients who have pain serious enough to require daily, around-the-clock opioid treatment and for which alternative treatment options are inadequate.

Following multiple complete response letters and additional studies, on February 13, 2018, Pain Therapeutics stated that the REMOXY ER NDA had been resubmitted. On August 6, 2018, Pain Therapeutics stated that it had received a Complete Response Letter from the FDA, which concluded that "The data submitted in [the] NDA do not support the conclusion that the benefits of [REMOXY] Extended-Release Capsules outweigh the risks." Pain Therapeutics further announced a strategic reorganization to align its resources on advancing its drug and diagnostic assets in Alzheimer's disease. While Pain Therapeutics has also indicated that they may appeal the FDA's decision, there can be no assurance that they will do so or that any such appeal will be successful.

ORADUR-ADHD Program

In August 2009, we entered into a development and license agreement with Orient Pharma Co., Ltd., a diversified multinational pharmaceutical, healthcare and consumer products company with headquarters in Taiwan, under which we granted to Orient Pharma development and commercialization rights in certain defined Asian and South Pacific countries to ORADUR-Methylphenidate ER Capsules (referred to by Orient Pharma as Methydur Sustained Release Capsules). We retain rights to North America, Europe, Japan and all other countries not specifically licensed to Orient Pharma.

Orient Pharma conducted a Phase 3, multi-center, randomized, double-blind, placebo-controlled, two-way cross-over study designed to demonstrate the efficacy and safety of ORADUR-Methylphenidate ER in children and adolescents with ADHD between the ages of 6 and 18 years. According to Orient Pharma, the study was conducted in Taiwan and enrolled 110 subjects, of which 100 evaluable subjects completed the study. For the primary efficacy endpoint, Orient Pharma observed a statistically significant difference between Methydur Sustained Release Capsules and Placebo treatments in the mean change of total score for the Swanson, Nolan, and Pelham-IV (SNAP-IV) teacher form ($p=0.0044$ for the intent to treat population and $p=0.0104$ for the per protocol population). Orient Pharma's safety analysis indicates that the incidence of adverse events with Methydur Sustained Release Capsules was similar to other approved methylphenidate products.

In September 2018, Orient Pharma informed us that it had obtained marketing authorization for Methydur Sustained Release Capsules from the Ministry of Health and Welfare in Taiwan. Methydur Sustained Release Capsules are indicated for the treatment of attention deficit hyperactivity disorder (ADHD) and will be available in three strengths (22 mg, 33 mg and 44 mg) in Taiwan. Orient Pharma also has stated that it expects to have Methydur Sustained Release Capsules commercially available in Taiwan in 2019, while seeking a partner in China and pursuing regulatory approvals in selected other countries where it has commercialization rights and a commercialization presence. We are seeking potential development and commercialization partners for ORADUR-Methylphenidate ER Capsules for major markets not licensed to Orient Pharma.

Other Programs

Depot injectable programs

In addition to biologic drugs, many traditional small molecule drugs have to be given by frequent injections, which is costly, inconvenient and may result in either unwanted side effects or suboptimal efficacy. We have active programs underway to improve our depot injectable systems and to apply those systems to various drugs and drug candidates, and have entered into a number of feasibility studies with biotechnology and pharmaceutical companies to test their products in our systems. The Relday program with Zogenix and the ophthalmic program with Santen are two projects which started as depot injectable feasibility projects and then matured into development and license agreements.

Product Revenues

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

- ALZET® osmotic pumps which are used for animal research;
- LACTEL® biodegradable polymers which are used by our customers as raw materials in their pharmaceutical and medical products; and
- certain key excipients that are included in Methydur and one excipient that is included in a currently 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 revenue related to collaborative research and development by 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 had a history of operating losses. At September 30, 2018, we had an accumulated deficit of $461.3 million. Our net loss was $2.7 million and $18.0 million for the three and nine months ended September 30, 2018, respectively. Our net losses were $3.7 million and $34.5 million for the years ended December 31, 2017 and 2016, respectively. 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 2018 as we experience higher research and development expenses related to DUR-928. We expect selling, general and administrative expenses in the fourth quarter of 2018 to be comparable to the third quarter of 2018. We do not anticipate meaningful revenues from our products in development, should they be approved, for at least the next twelve months. Therefore, 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 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, the recoverability of our long-lived assets, including goodwill and other intangible assets, accrued liabilities, contract research liabilities, inventories and stock-based compensation. Actual amounts could differ significantly from these estimates. For a description of our critical accounting policies and estimates affecting revenue from contracts with customers, see Note 1, "*Revenue Recognition*" to our unaudited condensed financial statements included in this Quarterly Report on Form 10-Q. Other than our critical accounting policies and estimates affecting revenue from contracts with customers, 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, 2017.

Results of Operations

Three and nine months ended September 30, 2018 and 2017

Collaborative research and development and other revenue

We recognize revenues from collaborative research and development activities and service contracts. Collaborative research and development 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 recognized from ratable recognition of upfront fees and milestone payments in connection with our collaborative agreements.

We expect our collaborative research and development and other revenue in the fourth quarter of 2018 to decrease compared to the third quarter of 2018 as we earned a $5.0 million milestone payment from Indivior upon NDA approval of PERSERIS in the third quarter of 2018. We expect our collaborative research and development and other revenue 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 are as follows (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Collaborator/Counterparty				
Indivior UK Limited (Indivior) (1)	$ 5,000	$ -	$ 5,000	$ -
Sandoz AG (Sandoz) (2)	-	3,846	-	4,615
Santen Pharmaceutical Co. Ltd. (Santen) (3)	-	85	1	234
Pain Therapeutics, Inc. (Pain Therapeutics)	-	4	-	109
Zogenix, Inc. (Zogenix) (4)	-	750	-	835
Others (5)	691	917	2,431	1,511
Total collaborative research and development and other revenue	$ 5,691	$ 5,602	$ 7,432	$ 7,304

(1) Amount related to a $5.0 million milestone payment earned in each of the three and nine months ended September 30, 2018, compared to zero for the corresponding periods in 2017.

(2) Amounts related to ratable recognition of upfront fees were zero for each of the three and nine months ended September 30, 2018, compared to $3.8 million and $4.6 million for the corresponding periods in 2017.

(3) Amounts related to ratable recognition of upfront fees were zero for each of the three and nine months ended September 30, 2018, compared to $48,000 and $153,000 for the corresponding periods in 2017.

(4) Amounts related to ratable recognition of upfront fees were zero for each of the three and nine months ended September 30, 2018, compared to $750,000 and $833,000 for the corresponding periods in 2017. In August 2017, the Company and Zogenix terminated the Development and License Agreement between us dated July 11, 2011 relating to the development and commercialization of Relday.

(5) Includes revenue recognized associated with our feasibility agreements for each of the three and nine months ended September 30, 2018 and 2017.

Product revenue

A portion of our revenues is derived from product sales, which include our ALZET mini pump product line, our LACTEL biodegradable polymer product line and certain excipients that are included in Methydur and in a currently marketed animal health product. Net product revenues were $2.3 million and $7.5 million in the three and nine months ended September 30, 2018, respectively, compared to $2.6 million and $9.8 million for the corresponding periods in 2017. The decreases in the three and nine months ended September 30, 2018 were primarily attributable to lower revenue from our LACTEL product line as a result of lower units sold, partially offset by higher revenue from our ALZET mini pump product line as a result of higher units sold compared to the corresponding periods in 2017.

Cost of product revenues

Cost of product revenues were $912,000 and $3.2 million for the three and nine months ended September 30, 2018, respectively, compared to $3.1 million and $5.6 million for the corresponding periods in 2017. The decreases in the cost of product revenue in the three and nine months ended September 30, 2018 were primarily the result of charges of approximately $2.0 million in the three and nine months ended September 30, 2017 associated with the write-down of an excipient in light of the failure to achieve the primary endpoint in the PERSIST clinical trial. Excluding the charges associated with the write-down of the excipient included in three and nine months ended September 30, 2017, the decreases in the cost of product revenue in the three and nine months ended September 30, 2018 were primarily the result of lower cost of goods sold related to our LACTEL product line arising from lower units sold, partially offset by higher cost of goods sold related to our ALZET product line arising from higher units sold compared to the corresponding period in 2017. Cost of product revenues and gross profit margin will fluctuate from period to period depending upon the product mix in a particular period and unit volumes sold. Stock-based compensation expense recognized related to cost of product revenues was $24,000 and $72,000 for the three and nine months ended September 30, 2018, respectively, compared to $27,000 and $83,000 for the corresponding periods in 2017.

We had 21 manufacturing employees as of September 30, 2018 compared with 22 as of September 2017. 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 $6.5 million and $19.6 million for the three and nine months ended September 30, 2018, respectively, compared to $8.4 million and $25.0 million for the corresponding periods in 2017. The decrease in the three months ended September 30, 2018 was primarily attributable to lower research and development costs associated with POSIMIR, depot injectable programs, ORADUR-ADHD, the Santen ophthalmic program, and REMOXY ER, partially offset by higher research and development costs associated with DUR-928 and other research programs compared to the corresponding period in 2017, as more fully discussed below. The decrease in the nine months ended September 30, 2018 was primarily attributable to lower research and development costs associated with POSIMIR, ORADUR-ADHD, the Santen ophthalmic program, REMOXY ER and other research programs, partially offset by higher research and development costs associated with DUR-928 and depot injectable programs compared to the corresponding period in 2017, as more fully discussed below. Stock-based compensation expense recognized related to research and development personnel was $238,000 and $929,000 for the three and nine months ended September 30, 2018, respectively, compared to $374,000 and $1.1 million for the corresponding periods in 2017. As of September 30, 2018, we had 47 research and development employees compared with 50 as of September 30, 2017. We expect research and development expenses in the near future to increase compared to the third quarter of 2018 as we expect to incur higher research and development expenses for DUR-928.

Research and development expenses associated with our major development programs approximate the following (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
DUR-928	$ 3,875	$ 3,153	$ 11,708	$ 9,755
POSIMIR	1,938	4,297	5,199	12,875
Depot injectable programs	597	760	2,284	1,704
ORADUR-ADHD	13	48	65	85
Santen ophthalmic program (1)	4	32	15	81
REMOXY ER (1)	2	5	13	101
Others	113	83	330	404
Total research and development expenses	$ 6,542	$ 8,378	$ 19,614	$ 25,005

(1) See Note 2 Strategic Agreements in the financial statements for more details about our agreements with Pain Therapeutics, and Santen.

DUR-928

Our research and development expenses for DUR-928 were $3.9 million and $11.7 million in the three and nine months ended September 30, 2018, respectively, compared to $3.2 million and $9.8 million for the corresponding periods in 2017. The increases in the three and nine months ended September 30, 2018 were primarily due to higher contract manufacturing expenses, higher clinical and non-clinical study expenses and higher employee-related expenses incurred for this drug candidate compared with the corresponding periods in 2017.

POSIMIR

Our research and development expenses for POSIMIR were $1.9 million and $5.2 million in the three and nine months ended September 30, 2018, respectively, compared to $4.3 million and $12.9 million for the corresponding periods in 2017. The decreases in the three and nine months ended September 30, 2018 were primarily due to lower clinical trial expenses and lower employee-related expenses for POSIMIR compared with the corresponding periods in 2017.

Depot injectable programs

Our research and development expenses for depot injectable programs were $597,000 and $2.3 million in the three and nine months ended September 30, 2018, respectively, compared to $760,000 and $1.7 million for the corresponding periods in 2017. The decrease in the three months ended September 30, 2018 were primarily due to lower employee-related costs for these programs compared with the corresponding period in 2017. The increase in the nine months ended September 30, 2018 was primarily due to higher employee-related costs and higher costs related to research supplies for these programs compared with the corresponding period in 2017.

ORADUR-ADHD

Our research and development expenses for ORADUR-ADHD were $13,000 and $65,000 in the three and nine months ended September 30, 2018, respectively, compared to $48,000 and $85,000 for the corresponding periods in 2017. The decreases in the three and nine months ended September 30, 2018 were primarily due to lower employee-related costs for the drug candidate compared with the corresponding periods in 2017.

Santen ophthalmic program

Our research and development expenses for the Santen ophthalmic program were $4,000 and $15,000 in the three and nine months ended September 30, 2018, respectively, compared to $32,000 and $81,000 for the corresponding periods in 2017. The decreases in the three and nine months ended September 30, 2018 were primarily due to decreased formulation development activities and lower employee-related costs associated with this drug candidate compared with the corresponding periods in 2017.

REMOXY ER

Our research and development expenses for REMOXY ER were $2,000 and $13,000 in the three and nine months ended September 30, 2018, respectively, compared to $5,000 and $101,000 for the corresponding periods in 2017. The decreases in the three and nine months ended September 30, 2018 were primarily due to lower employee-related costs for REMOXY ER compared with the corresponding periods in 2017.

Other DURECT research programs

Our research and development expenses for all other programs were $113,000 and $330,000 in the three and nine months ended September 30, 2018, respectively, compared to $83,000 and $404,000 for the corresponding periods in 2017, respectively. The increase in the three months ended September 30, 2018 was primarily due to higher employee-related costs incurred as well as higher outside expenses associated with these programs compared with the corresponding period in 2017. The decrease in the nine months ended September 30, 2018 was primarily due to lower employee-related costs incurred as well as lower outside expenses associated with these programs compared with the corresponding period in 2017.

We expect our research and development expenses in the near future to increase compared to the third quarter of 2018 as we expect to incur higher research and development expenses for DUR-928. 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 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, 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 estimated 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 cost 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 $2.9 million and $8.9 million for the three and nine months ended September 30, 2018, respectively, compared to $3.1 million and $9.9 million for the corresponding periods in 2017. The decrease in selling, general and administrative expenses in the three months ended September 30, 2018 was primarily due to lower legal and patent related expenses compared with the corresponding period in 2017. The decrease in selling, general and administrative expenses in the nine months ended September 30, 2018 was primarily due to an advisory fee incurred in the nine months ended September 30, 2017 that related to the licensing agreement with Sandoz. Stock-based compensation expense recognized related to selling, general and

administrative personnel was $277,000 and $838,000 for the three and nine months ended September 30, 2018, respectively, compared to $301,000 and $789,000 for the corresponding periods in 2017.

We had 22 selling, general and administrative employees as of September 30, 2018 compared with 24 as of September 2017. We expect selling, general and administrative expenses in the near future to be comparable to the second quarter of 2018.

Other income (expense). Interest and other income was $234,000 and $632,000 for the three and nine months ended September 30, 2018, respectively, compared to $605,000 and $680,000 for the corresponding periods in 2017. The decrease in interest and other income in the three and nine months ended September 30, 2018 was primarily the result of a gain of $500,000 from selling certain intellectual property rights in the three and nine months ended September 30, 2017. This transaction was not part of our ordinary course of business and therefore was recorded as a gain from selling intellectual property rights in other income in the three and nine months ended September 30, 2017. Excluding this transaction, the increases in interest and other income in the three and nine months ended September 30, 2018 were primarily the result of higher interest income generated from our investments as a result of higher yields and higher average balances in the three and nine months ended September 30, 2018 compared with the corresponding periods in 2017.

Interest expense was $661,000 and $1.9 million for the three and nine months ended September 30, 2018, respectively, compared to $619,000 and $1.8 million for the corresponding periods in 2017. The increases in interest and other expense in the three and nine months ended September 30, 2018 were primarily due to higher interest rates associated with the term loan compared with the corresponding periods in 2017.

Liquidity and Capital Resources

We had cash, cash equivalents and investments totaling $41.5 million at September 30, 2018 compared to $36.9 million at December 31, 2017. These balances include $150,000 of interest-bearing marketable securities classified as restricted investments on our balance sheets as of September 30, 2018 and December 31, 2017. The increase in cash, cash equivalents and investments during the nine months ended September 30, 2018 was primarily due to the receipt of $18.4 million of cash from the sale of our common stock and from exercises of stock options and purchases under our employee stock purchase plan, and from payments received from collaboration partners and customers, partially offset by ongoing operating expenses and interest payments.

We used $13.6 million of cash in operating activities in the nine months ended September 30, 2018 compared to $6.1 million received for the corresponding period in 2017. The increase in cash used in operating activities in the nine months ended September 30, 2018 was primarily due to decreased payments received from collaboration partners and customers as we received the $20.0 million upfront fee from Sandoz in the nine months ended September 30, 2017, partially offset by changes in accounts receivable, prepaid expenses and other assets, and accrued and other liabilities in the nine months ended September 30, 2018 compared to the corresponding period in 2017.

We received $4.2 million of cash from investing activities for the nine months ended September 30, 2018 compared to $13.7 million for the corresponding period in 2017. The decrease in cash received from investing activities was primarily due to a decrease in proceeds from maturities of available-for-sale securities for the nine months ended September 30, 2018 compared to the corresponding period in 2017. We anticipate incurring capital expenditures of approximately $100,000 in 2018 to purchase research and development and other capital equipment.

We received $18.3 million of cash from financing activities for the nine months ended September 30, 2018 compared to $10.1 million for the corresponding period in 2017. The increase in cash received from financing activities was primarily due to higher net proceeds received from issuances of common stock in the nine months ended September 30, 2018 compared with the corresponding period in 2017. During the nine months ended September 30, 2018, we raised net proceeds (net of commission) of approximately $16.8 million from the sale of 9.6 million shares of common stock at a weighted average price of $1.80 per share in the open market through our Controlled Equity Offering sales agreement with Cantor Fitzgerald, entered into in November 2015.

In November 2015, we filed a shelf registration statement on Form S-3 with the SEC, which upon being declared effective in November 2015, allowed us to offer up to $125.0 million of securities from time to time in one or more public offerings, inclusive of $40.0 million of common stock which we were permitted to sell pursuant to the 2015 Sales Agreement entered into in November 2015 with Cantor Fitzgerald, acting as agent. As of September 30, 2018, approximately 24.6 million shares of common stock were sold through the 2015 Sales Agreement for an aggregate purchase price of approximately $39.5 million. In August 2018, we filed a new shelf registration statement on Form S-3 with the SEC, which upon being declared effective in October 2018, terminated the November 2015 registration statement and allowed us 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 additional shares of common stock which we may sell, subject to certain limitations, under the 2015 Sales Agreement through Cantor Fitzgerald, acting as agent. As of November 2, 2018, no sales had been made pursuant to the October 2018 registration statement.

We anticipate that cash used in operating activities in the fourth quarter of 2018 will increase compared to the third quarter of 2018 due to the $5 million milestone payment received by DURECT from Indivior related to the July 2018 NDA approval of PERSERIS in the third quarter of 2018.

During the nine months ended September 30, 2018, there were significant changes in our commercial commitments and contractual obligations due to the extension of our three building facility leases (see Note 6 of the financial statements). Subsequently, on November 1, 2018, we and Oxford Finance entered into a Second Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from December 1, 2018 to June 1, 2020 and the final maturity date from August 1, 2020 to November 1, 2022. If we elect 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 interest rate and the final payment remain unchanged, and we paid Oxford Finance a Second Amendment fee of $900,000.

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 the date the financial statements are filed. We may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding. Additionally, we do not expect to generate significant revenues from our pharmaceutical products currently under development for at least the next twelve months, if at all. Depending on whether we enter into additional collaborative agreements in the near term and the extent to which we earn milestone revenues, we may be required to raise additional capital through a variety of sources, 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 in the near term, will earn milestone 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.

Contractual Obligations and Commitments

In aggregate, we are required to make future payments pursuant to our existing contractual obligations as follows (in thousands):

Contractual Obligations	Three months ended December 31, 2018	2019	2020	2021	2022	2023 and thereafter	Total
Capital lease (1)	$ 4	$ 7	$ 4	$ 1	$ —	$ —	$ 16
Term loan (1)	1,389	1,941	7,127	9,066	8,962	—	28,485
Purchase commitments (2)	500	—	—	—	—	—	500
Operating lease obligations	491	2,122	2,200	2,126	1,991	2,245	11,175
Total contractual cash obligations	$ 2,384	$ 4,070	$ 9,331	$ 11,193	$ 10,953	$ 2,245	$ 40,176

(1) Includes the amendment fee, principal and interest payments and assumes no acceleration of obligations pursuant to the November 1, 2018 Second Amendment to the Loan Agreement.

(2) Recorded as an accrued liability on our balance sheet at September 30, 2018.

Off-Balance Sheet Arrangements

As of September 30, 2018, we did not have any off-balance sheet arrangements, as defined under SEC Regulation S-K Item 303(a)(4)(ii).

Item 3. Quantitative and Qualitative Disclosures about Market Risk

During the nine months ended September 30, 2018, there have been no significant changes in market risks as disclosed in our Annual Report on Form 10-K for the year ended December 31, 2017.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures: The Company's principal executive and 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 Form 10-Q. Based on that evaluation, the Company's principal executive and 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 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.

Risks Related To Our Business

New chemical entities derived from our Epigenetic Regulator Program, which is in the early stages of development, may require more time and resources for development, testing and regulatory approval than our Drug Delivery Program product candidates, and may not result in any approval or viable commercial products

Our Epigenetic Regulator Program is in the early stages of development, involves a novel therapeutic approach and new chemical entities, requires significant further research and development and regulatory approvals and is subject to the risks of failure inherent in the development of products based on innovative approaches. New chemical entities derived from our Epigenetic Regulator Program are molecules that have not previously been approved and marketed as therapeutics, unlike product candidates in our Drug Delivery Programs, in which we apply our formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which we aim to improve in some manner through a new formulation. As a result, the product candidates from our Epigenetic Regulator Program may face greater risk of unanticipated safety issues or other side-effects, or may not demonstrate efficacy. Further, the regulatory pathway for our new chemical entities may be more demanding than that for product candidates under our Drug Delivery Programs, for which we may be able to leverage existing data under Section 505(b)(2) of the Act to reduce development risk, time and cost. For example, we have yet to define the therapeutic dose or dosing regimen for DUR-928, the first drug candidate in our Epigenetic Regulator Program.

Also, because our Epigenetic Regulator Program is in early stages, we have not defined with precision those indications we wish to pursue, each of which may have unique challenges. If the first indications pursued do not show positive results, the credibility of any product candidate from this program may be tarnished, even if the molecule might be effective for other indications. Our decisions regarding which indications to pursue may cause us to fail to capitalize on indications that could have given rise to viable commercial products and profitable market opportunities.

Early indications of activity from Phase 1 clinical trials of DUR-928 may not predict therapeutic efficacy

While Phase 1 clinical trials of DUR-928 have shown a reduction of certain biomarkers after a single oral dose in patients with NASH or CKD, these trials are designed to assess the safety of DUR-928, and are not designed to evaluate its efficacy. Although Phase 1 clinical trials of DUR-928 have demonstrated that DUR-928 can lead to the reduction of certain biomarkers, such as statistically significant reductions from baseline in the levels of both full-length and cleaved cytokeratin-18 (CK-18), bilirubin, high sensitivity C-Reactive Protein (hsCRP) and IL-18 in NASH patients, changes in such biomarkers may ultimately not be correlated with treatment or improvement in the associated disease, and there is a risk that DUR-928 may not demonstrate therapeutic efficacy, despite apparent improvements in biomarker levels. Additional controlled clinical trials will be required to evaluate the safety and efficacy of DUR-928 to treat any indication, including NASH, psoriasis and CKD. There can be no assurance that these studies will demonstrate the safety or efficacy of DUR-928 in a statistically significant manner. The failure of DUR-928 to show efficacy or if safety signals emerge in ongoing and future clinical trials would significantly harm our business.

Plans and prospects for POSIMIR are uncertain following the failure of the PERSIST trial to achieve its primary endpoint

The failure of the PERSIST trial for POSIMIR to achieve its primary endpoint gives Sandoz a right to terminate our agreement with them on thirty days' notice. Sandoz may elect to terminate the agreement, in which case we will not receive any milestone or royalty payments under the agreement and will be responsible for commercialization of POSIMIR in the United States, if approved. Even if Sandoz does not terminate the agreement, we remain responsible for obtaining approval of POSIMIR from the Food and Drug Administration. The decision whether to continue the development of POSIMIR and seek regulatory approval will require further analysis of the PERSIST trial data and other clinical data for POSIMIR, as well as possible regulatory approval strategies. We may elect to terminate development of POSIMIR. If we elect to continue to develop and seek approval for POSIMIR, we may be required to make a larger investment than previously planned, which would limit the funds available for other product

development activities or require us to raise capital earlier than anticipated. It may also take longer to receive FDA approval than anticipated, and such approval may never occur.

If we experience delays or difficulties in the enrollment of subjects in clinical trials, our product development expenses may increase, clinical trial data could be delayed and receipt of necessary regulatory approvals could be delayed or prevented

Successful and timely completion of clinical trials will require that we enroll a sufficient number of subjects. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population and the ability of clinical sites to successfully recruit subjects to participate in clinical trials. 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 our drug candidates if we are unable to locate and enroll a sufficient number of eligible subjects to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. It is possible that the specific requirements by the FDA for our patients to be included in these trials may make the trials more difficult to conduct or may significantly extend the time required for enrollment of these trials.

We cannot predict how successful we will be at enrolling subjects in our clinical trials. Subject enrollment is affected by other factors including:

- the eligibility criteria for the trial in question;
- the prevalence and incidence of the conditions being studied in the clinical trials;
- 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 patients from other clinical trials;
- the willingness of potential clinical trial subjects to provide informed consent to participate in the trial;
- the patient referral practices of physicians;
- the ability to monitor subjects adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective subjects.

Our inability to enroll a sufficient number of subjects 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 progression, which would cause the value of our company to decline and limit our ability to obtain additional financing.

The FDA 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 FDA's requirements, and thus our product candidates may not be approved for marketing. For example, the Phase 3 PERSIST trial for POSIMIR did not meet its primary efficacy endpoint of reduction in pain on movement over the first 48 hours after surgery as compared to standard bupivacaine HCl. In addition, during the review process, the FDA may request more information regarding the safety of our product candidates, as they have in their Complete Response Letter for POSIMIR, 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. During the review process, the FDA may also request more information regarding the chemistry, manufacturing or controls related to our product candidates or to abuse deterrent properties of opioid product candidates, as they have in their Complete Response Letters for REMOXY ER, 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. Additionally, even if our product candidates receive FDA approval, the FDA may require that we conduct additional clinical studies after such approval, place limitations on our products in applicable labels, require marketing under a REMS program, delay approval to market our products or limit the use of our products, which may harm our business and results of operations.

The path to regulatory approval of DUR-928 is uncertain.

We are currently developing DUR-928 in several indications, including AH and PSC, with plans to develop DUR-928 for other indications such as psoriasis and NASH. In several of these indications, there are no currently approved drugs. Accordingly, we will have to interact with the FDA and other regulatory agencies regarding important aspects of the clinical development program, including the size of clinical trials, the specific primary and secondary endpoints for the clinical trials, inclusion and exclusion criteria, stopping rules and other matters. This uncertainty may make it difficult to predict the timing or expense required to obtain regulatory approval for DUR-928. We also may need to revise our clinical development plans after trials have commenced or been completed, which could add to the time and expense associated with the clinical development of DUR-928. If we are unable to reach agreement with the FDA regarding clinical development plans for DUR-928, we may curtail or limit our development activities for this product candidate.

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

In July 2016, we entered into a Loan and Security Agreement (the 2016 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 a 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 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. The 2016 Loan Agreement provides for a floating interest rate (7.95% initially and 9.57% as of September 30, 2018) based on an index rate plus a spread, a $150,000 facility fee that was paid at closing and an additional payment equal to 9.25% of the principal amount of the term loan, which is due when the term loan becomes due or upon the prepayment of the facility. If we elect to prepay the loan, there is also a prepayment fee between 1% and 3% of the principal amount of the term loan depending on the timing of prepayment. In February 2018, we and Oxford Finance entered into a First Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from March 1, 2018 to December 1, 2018 and to increase the additional payment due when the term loan becomes due or upon the prepayment of the facility from 9.25% of the principal amount of the term loan to 10% of such amount. The interest rate and the maturity date remain unchanged, and we paid Oxford Finance a loan modification fee of $100,000. In November 2018, we and Oxford Finance entered into a Second Amendment of the Loan Agreement, which modified the terms of the Loan Agreement to change the first principal payment date from December 1, 2018 to June 1, 2020 and the final maturity date from August 1, 2020 to November 1, 2022. If we elect 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 interest rate and the final payment remain unchanged, and we paid Oxford Finance a Second Amendment fee of $900,000 on November 1, 2018. Our debt repayment obligations under the 2016 Loan Agreement, as amended, may prove a burden to the Company as they become due, particularly following the expiration of the interest-only period.

The 2016 Loan Agreement contains customary events of default, including, among other things, our failure to fulfill certain of our obligations under the 2016 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 2016 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 2016 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 2016 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 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 complete the research, development and

clinical testing of our pharmaceutical product candidates. We will require additional funds for these purposes, to establish additional clinical- and commercial-scale manufacturing arrangements and facilities, and to provide for the marketing and distribution of our product candidates. 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, we may have to delay, reduce the scope of or eliminate one or more of our research or development programs which would materially harm our business, financial condition and results of operations.

We believe that our cash, cash equivalents and investments will be adequate to satisfy our capital needs for at least the next 12 months from the date the financial statements are filed. However, our actual capital requirements will depend on many factors, including:

- success in entering into collaboration agreements and achieving milestones under such agreements;
- the continuation of our collaborative agreements that provide financial funding for our activities;
- regulatory actions with respect to our and our collaborators' product candidates;
- 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 clearance;
- costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims;
- costs of developing sales, marketing and distribution channels and our ability and that of our collaborators to sell our pharmaceutical product candidates;
- costs involved in establishing manufacturing capabilities for clinical and commercial quantities of our product candidates;
- competing technological and market developments;
- market acceptance of our product candidates;
- any failure to comply with the covenants in our debt instruments that results in acceleration of repayment obligations;
- 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 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 or pharmaceutical 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, resulting in delays in generating future product revenue.

We do not control development or commercialization of PERSERIS

We rely on Indivior for the commercialization of PERSERIS. There can be no assurance that Indivior will launch PERSERIS commercially or it will obtain market acceptance and meaningful sales. If Indivior does not launch and successfully commercialize PERSERIS, we will not receive earn-out payments under our agreement with them or those earn-out payments may be limited.

REMOXY ER and PERSERIS may not be commercialized

We are dependent on Pain Therapeutics to obtain FDA approval of REMOXY ER. On August 6, 2018, following multiple Complete Response Letters, Pain Therapeutics stated that it had received a Complete Response Letter from the FDA, which concluded that "The data submitted in [the] NDA do not support the conclusion that the benefits of [REMOXY] Extended-Release Capsules outweigh the risks." Pain Therapeutics further announced a strategic reorganization to align its resources on advancing its drug and diagnostic assets in Alzheimer's disease. Pain Therapeutics has also indicated that it may appeal the FDA's decision. We cannot control whether Pain Therapeutics will continue to pursue regulatory approval, commercialization or licensing of REMOXY ER, or if they do so, whether REMOXY ER will ever be approved or commercially successful. If they do not, we would not realize any future income from our agreement with Pain Therapeutics.

We rely on Indivior for the commercialization of PERSERIS. There can be no assurance that Indivior will launch PERSERIS commercially or it will obtain market acceptance and meaningful sales. If Indivior does not launch and successfully commercialize PERSERIS, we will not receive earn-out payments under our agreement with them or those earn-out payments may be limited.

Development of our pharmaceutical product candidates is not complete, and we cannot be certain that our product candidates will be able to be commercialized

To be profitable, we or our third-party collaborators must successfully research, develop, obtain regulatory approval for, manufacture, introduce, market and distribute our pharmaceutical product candidates under development. For each product candidate that we or our third-party collaborators intend to commercialize, we must successfully meet a number of critical developmental milestones for each disease or medical condition targeted, including:

- with respect to each new chemical entity, determining appropriate indication(s);
- with respect to our Drug Delivery Program product candidates, selecting and developing a drug delivery technology to deliver the proper dose of drug over the desired period of time;
- determining the appropriate route of administration and drug dosage for use in the pharmaceutical product candidate;
- developing drug compound formulations that will be tolerated, safe and effective and that will be compatible with the active pharmaceutical agent;
- demonstrating the drug formulation will be stable for commercially reasonable time periods;
- demonstrating through clinical trials that the drug formulation is safe and effective in patients for the intended indication at an achievable dose and that the drug's benefits outweigh its risks;
- demonstrating abuse deterrent properties to the satisfaction of the FDA for certain products for which abuse-deterrence is considered an important feature by the FDA, and
- completing the manufacturing development and scale-up to permit manufacture of the pharmaceutical product candidate in commercial quantities and at acceptable cost.

The time frame necessary to achieve these developmental milestones for any individual product is long and uncertain, and we may not successfully complete these milestones for any of our products in development. Except for marketing authorization for Orient Pharam's distribution of Methydur Sustained Release Capsules in Taiwan development is incomplete for all product candidates in our development programs, including DUR-928. We may not be able to finalize the design or formulation of any of these product candidates. Further, although we believe our design and formulation of POSIMIR and ORADUR-Methylphenidate ER to be substantially complete, there can be no assurance that additional developments will not be required prior to any regulatory approval of these products. In addition, we may select components, solvents, excipients or other ingredients to include in our product candidates that have not been previously approved for use in pharmaceutical products, which may require us or our collaborators to perform additional studies and may delay clinical testing and regulatory approval of our product candidates. Even after we complete the design of a product candidate, the product candidate must still complete required clinical trials and additional safety testing in animals before approval for commercialization. We are continuing testing and development of our product candidates and may explore possible design or formulation changes to address issues of safety, manufacturing efficiency and performance. We or our collaborators may not be able to complete development of any product candidates that will be safe and effective and that will have a commercially reasonable treatment and storage period. If we or our third-party collaborators are unable to complete development of DUR-928, POSIMIR, ORADUR-Methylphenidate ER (outside of the territories licensed to OP Pharma) or other product candidates, we will not be able to earn revenue from them, which would materially harm our business.

We or our third-party collaborators must show the safety and efficacy of our drug candidates in animal studies and human clinical trials to the satisfaction of regulatory authorities before they can be sold; failure to obtain approvals for DUR-928, REMOXY ER, POSIMIR or our other product candidates would significantly harm our business, prospects and financial condition

Before we or our third-party collaborators can obtain government approval to sell any of our pharmaceutical product candidates, we or they, as applicable, must demonstrate through laboratory performance studies and safety testing, nonclinical (animal) studies and clinical (human) trials that each system is safe and effective for human use and that the benefits outweigh the risks for each targeted indication. The clinical development status of our major development programs is as follows:

- DUR-928—In 2015, we completed initial Phase 1 human trials of DUR-928 when orally administered and when administered through injection to a total of over 75 healthy volunteers. These trials evaluated the safety, tolerability and pharmacokinetics of DUR-928 when administered with a single dose and then with multiple doses. The high doses in these studies resulted in plasma levels greater than 100-fold higher than endogenous levels of DUR-928, and DUR-928 was observed to be well tolerated at all doses, with no severe or serious drug-related adverse events reported. In these

studies, there was no accumulation in plasma concentrations observed with repeated dosing, and there were dose related increases in plasma concentrations. In 2016 and 2017, we conducted a single-ascending-dose Phase 1b clinical trial with DUR-928 in patients with nonalcoholic steatohepatitis (NASH). This study was conducted in Australia in successive cohorts evaluating single-dose levels (first a low dose and then a high dose) of orally administered DUR-928. Both cohorts consisted of 10 NASH patients and 6 matched control subjects. One patient (with a prior history of arrhythmia and an ongoing viral infection) in the high dose cohort experienced a serious adverse event (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 the low and high dose cohorts, the PK parameters were comparable between the NASH patients and the matched control subjects. In addition, the systemic exposure following the low and high doses of DUR-928 was dose dependent. While this study was not designed to assess efficacy, we observed a reduction of certain biomarkers after a single oral dose of DUR-928. Exploratory biomarker analysis indicated that a single oral dose of DUR-928 resulted in statistically significant reductions from baseline in the levels of both full-length and cleaved cytokeratin-18 (CK-18), bilirubin, hsCRP and IL-18. We also conducted in Australia a Phase 1b open-label, single-ascending-dose study in patients with impaired kidney function (stage 3 and 4 chronic kidney disease) and matched control patients with injected DUR-928. This study was conducted in two successive cohorts (first a low dose and then a high dose) evaluating the safety and PK of single-dose intramuscular injected DUR-928. The low dose cohort consisted of 6 kidney function impaired patients and 3 matched control subjects; the high dose cohort consisted of 5 kidney function impaired patients and 3 matched control subjects. In this trial, DUR-928 was well tolerated among all subjects and the PK parameters between the kidney function impaired patients and the matched control subjects were comparable. While the number of subjects involved was small and not designed to assess efficacy, we did observe decreases in bilirubin and CK-18 when those levels were meaningfully elevated pre-treatment, although these results were not statistically significant. We are currently conducting a Phase 2a trial in patients with primary sclerosing colangitis (PSC) and a Phase 2a trial in patients with Alcoholic Hepatitis. In addition, we conducted an exploratory Phase 1b trial in psoriasis patients (9 evaluable patients) in Australia. The Phase 1b trial was conducted with intralesional micro injections of DUR-928, and we feel the results warrant further investigation. As a result, we plan to evaluate topical application of DUR-928 in a future Phase 2 proof-of-concept trial. We are planning to conduct a clinical trial in NASH patients with orally-administered DUR-928 beginning in the first half of 2019. There can be no assurance that biological activity demonstrated in previous animal disease models will also be seen in human trials, or that any clinically relevant biological activity will be seen in humans. There can also be no assurance that current and future planned trials will be conducted on the timetable anticipated, that further human trials will not identify safety issues, or that we will be able to successfully develop DUR-928 to obtain marketing approval by the FDA or other regulatory agencies.

- PERSERIS—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. On July 27, 2018, Indivior announced that the FDA had approved the NDA for PERSERIS. On November 1, 2018, Indivior stated that they are preparing a full promotional launch of PERSERIS with a field force of 40 to 60 representatives, contingent upon the preliminary injunction against Dr. Reddy's Laboratories being upheld by the U.S. Court of Appeals for the Federal Circuit. Indivior further stated that they will be making PERSERIS available in the U.S. in Q4 2018 to begin generating product awareness and trial.
- POSIMIR—In April 2013, we submitted a new drug application as a 505(b)(2) application, which relies in part on the FDA's findings of safety and effectiveness of a reference drug. In February 2014, we received a Complete Response Letter from the FDA. Based on the Complete Response Letter and subsequent communications with the FDA, we conducted a new Phase 3 clinical trial consisting of patients undergoing laparoscopic cholecystectomy (gallbladder removal) surgery to further evaluate the benefits and risks of POSIMIR. We began recruiting patients for this trial in November 2015 comparing POSIMIR to placebo. Based on advice from the FDA received subsequent to the start of the trial, in April 2016, we decided to amend the PERSIST trial including by incorporating standard bupivacaine HCl as an active control. Starting in August 2016, we began implementing Part 2 of the PERSIST trial to evaluate POSIMIR against standard bupivacaine HCl rather than placebo as we had been doing in Part 1. Additionally, we switched in Part 2 the primary efficacy endpoint (pain reduction on movement) from 0-72 hours after surgery to 0-48 hours after surgery. Assessing pain reduction on movement from 0-72 hours became the key secondary efficacy endpoint and other efficacy endpoints, including 72-hour opioid use, remained the same. In October 2017, we reported that PERSIST, the Phase 3 clinical trial for POSIMIR, did not meet its primary efficacy endpoint of reduction in pain on movement over the first 48 hours after surgery as compared to standard bupivacaine HCl. While results trended in favor of POSIMIR versus the comparator, they did not achieve statistical significance. We continue to evaluate and consider potential next steps with the program. There can be no assurance that Sandoz will continue as our commercial partner for POSIMIR in the United States, that we will continue to develop POSIMIR or that POSIMIR will ever successfully obtain regulatory approval from the FDA.
- ORADUR-ADHD—In 2017, Orient Pharma, our licensee in defined Asian and South Pacific countries, completed a Phase 3, multi-center, randomized, double-blind, placebo controlled, two-way cross-over study designed to observe the

efficacy and safety of ORADUR-Methylphenidate ER Capsules (referred to by Orient Pharma as Methydur Sustained Release Capsules) in children and adolescents with ADHD age 6 to 18 years old. According to Orient Pharma, the study was conducted in Taiwan and enrolled 110 subjects, of which 100 evaluable subjects completed the study. For the primary efficacy endpoint, Orient Pharma observed a statistically significant difference between Methydur Sustained Release Capsules and Placebo treatments in the mean change of total score for the Swanson, Nolan, and Pelham-IV (SNAP-IV) teacher form (p=0.0044 for the intent to treat population and p=0.0104 for the per protocol population). Orient Pharma's safety analysis indicates that the incidence of adverse events with Methydur Sustained Release Capsules was similar to other approved Methylphenidate products. In September 2018, Orient Pharma informed DURECT that it has obtained marketing authorization for Methydur Sustained Release Capsules from the Ministry of Health and Welfare in Taiwan. Methydur Sustained Release Capsules are indicated for the treatment of attention deficit hyperactivity disorder (ADHD) and will be available in three strengths (22 mg, 33 mg and 44 mg) in Taiwan. Orient Pharma also has stated that it expects to have Methydur Sustained Release Capsules commercially available in Taiwan in 2019, while seeking a partner in China and pursuing regulatory approvals in selected other countries where it has commercialization rights and a commercialization presence. We are seeking development and commercialization partners for the major markets not licensed to Orient Pharma. There can be no assurance that we will be able to successfully develop ORADUR-Methylphenidate ER Capsules to obtain marketing approval by the U.S. FDA or other regulatory agencies, nor is there any assurance that we will be able to find a collaborator with respect to the development and commercialization of this drug candidate for the territories not licensed to Orient Pharma or that Orient Pharma will commercially launch Methydur Sustained Release Capsules in Taiwan or other of its Territories in a timely manner, or at all, or that if launched, it will obtain market acceptance and/or meaningful sales.

- REMOXY ER—Following multiple complete response letters and additional studies, including on abuse-deterrence, Pain Therapeutics resubmitted the NDA for REMOXY ER in February 2018. On August 6, 2018, Pain Therapeutics stated that it had received a Complete Response Letter from the FDA, which concluded that "The data submitted in [the] NDA do not support the conclusion that the benefits of [REMOXY] Extended-Release Capsules outweigh the risks." Pain Therapeutics further announced a strategic reorganization to align its resources on advancing its drug and diagnostic assets in Alzheimer's disease. While Pain Therapeutics has also indicated that they may appeal the FDA's decision, there can be no assurance that they will do so or that any such appeal will be successful. There can be no assurance that Pain Therapeutics will continue development of REMOXY ER, that it will successfully obtain marketing approval by the FDA or any other regulatory agency on a timely basis or at all, or that Pain Therapeutics will obtain a commercialization partner.

We are currently in the clinical, preclinical or research stages with respect to all of our biopharmaceutical product candidates under development except with respect to Methydur in Taiwan. We plan to continue extensive and costly tests, clinical trials and safety studies in animals to assess the safety and effectiveness of our product candidates. These studies include laboratory performance studies and safety testing, clinical trials and animal toxicological studies necessary to support regulatory approval of development products in the United States and other countries of the world. These studies are costly, complex and last for long durations, and may not yield data supportive of the safety or efficacy of our drug candidates or required for regulatory approval.

Certain of our drug candidates that may be developed, including REMOXY ER, are subject to mandatory Risk Evaluation and Mitigation Strategy (REMS) programs, which could delay the approval of these drug candidates, reduce demand for them, and increase the cost, burden and liability associated with their commercialization

For several years, FDA has required companies engaged in manufacturing and sales of opioid products to have a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of the drugs continue to outweigh the risks. The affected opioid drugs include brand name and generic products and are formulated with the active ingredients fentanyl, hydromorphone, methadone, morphine, oxycodone, and oxymorphone. All manufacturers of long-acting and extended-release opioids must ensure that training is provided to prescribers of these medications and develop information that prescribers can use when counseling patients about the risks and benefits of opioid use. The FDA has also announced safety labeling changes and post-market study requirements for extended-release and long-acting opioid analgesics (ER/LA opioids). The updated class-wide labeling changes state that ER/LA opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The updated indication further clarifies that, because of the risks of addiction, abuse, and misuse, even at recommended doses, and because of the greater risks of overdose and death, these drugs should be reserved for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain; ER/LA opioid analgesics are not indicated for as-needed pain relief. Recognizing that more information is needed to assess the serious risks associated with long-term use of ER/LA opioids, the FDA is requiring the drug companies that make these products to conduct further post-market studies and clinical trials. These changes may result in a decrease in prescriptions for this class of drugs and will increase the costs borne by manufacturers of ER/LA opioids. More recently, in February 2016, the FDA announced a comprehensive action plan to take concrete steps towards reducing the impact of opioid abuse on American families and communities. As part of this plan, the agency will review product and labelling decisions and re-examine the risk-benefit paradigm for opioids.

Certain of our drug candidates that may be developed, including REMOXY ER, are subject to the REMS requirement. The FDA's REMS requirements have been evolving, and until the contours of required REMS programs are established by the FDA and understood by drug developers and marketers such as ourselves and our collaborators, and until the results of the FDA's recently announced initiatives are known, there may be delays in marketing approvals for these drug candidates. In addition, there may be increased cost, administrative burden and potential liability associated with the marketing and sale of these types of drug candidates subject to the REMS requirement, as well as decreased demand resulting from new labeling requirements, which could negatively impact the commercial benefits to us and our collaborators from the sale of these drug candidates.

We depend to a large extent on third-party collaborators, and we have limited or no control over the development, sales, distribution and disclosure for our pharmaceutical product candidates which are the subject of third-party collaborative or license agreements

Our performance depends to a large extent on the ability of our third-party collaborators to successfully develop and obtain approvals for our pharmaceutical product candidates. We have entered into agreements with Sandoz, Indivior, Pain Therapeutics, Santen, Orient Pharma and others under which we granted such third parties the right to develop, apply for regulatory approval for, market, promote or distribute POSIMIR, REMOXY ER and other 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 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 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 collaborations regarding our product candidates 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) by providing notice. For example, in July 2017, we were notified by Impax that they were terminating our agreement with respect to ELADUR, and in August 2017, we mutually agreed with Zogenix to terminate our agreement with respect to Relday. In both instances, the product rights reverted to us. Sandoz also has the right to terminate our agreement with them for commercialization of POSIMIR after a specified notice period. 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 to enter into agreements with other third parties for use of the assets that were subject to the terminated agreement. Termination of our agreements with Sandoz, Pain Therapeutics, Santen or Orient Pharma could have similar effects.

Our revenues depend on collaboration agreements with other companies. If we are unable to enter into new agreements or meet our obligations or manage our relationships with our collaborators under these agreements our revenues may decrease. Acquisitions of our collaborators can be disruptive

Our revenues are 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. We have seen recent declines in revenues associated with our existing collaboration agreements, which reflect the current development stage of the product candidates subject to those agreements, and our collaborator's decreased needs for our services. We do not expect our collaboration revenues to increase unless we 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 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 under collaborations. 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, including our agreements with Sandoz with respect to POSIMIR, Pain

Therapeutics with respect to REMOXY ER, Orient Pharma with respect to ORADUR-Methylphenidate ER, and Santen with respect to an ophthalmic product 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, and if any of our collaborative agreements are terminated or delayed, our anticipated revenues may be reduced or not materialize, and our products in development related to those agreements may not be commercialized.

Our cash flows are likely to differ from our reported revenues

Our revenues will likely differ from our cash flows from revenue-generating activities. Upfront payments received upon execution of collaborative agreements are recorded as deferred revenue and generally recognized on a straight-line basis over the period of our continuing involvement with the third-party collaborator pursuant to the applicable agreement. The period of continuing involvement may also be revised on a prospective basis. As of September 30, 2018, we had $826,000 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.

Our revenues also depend on milestone payments based on achievements by our third-party collaborators. Failure of such collaborators to attain such milestones would result in our not receiving additional revenues

In addition to payments based on our performance of research and development activities, our revenues also depend on the attainment of milestones set forth in our collaboration agreements. Such milestones are typically related to development activities or sales accomplishments. While our involvement is generally necessary to the achievement of development-based milestones, the performance of our third-party collaborators is also generally required to achieve those milestones. Under our third-party collaborative agreements, our third party collaborators will take the lead in commercialization activities and we are typically not involved in the achievement of sales-based milestones. Therefore, we are even more dependent upon the performance of our third-party collaborators in achieving sales-based milestones. To the extent we and our third-party collaborators do not achieve such development-based milestones or our third-party collaborators do not achieve sales-based milestones, we will not receive the associated revenues, which could harm our financial condition and may cause us to defer or cut-back development activities or forego the exploitation of opportunities in certain geographic territories, any of which could have a material adverse effect on our business.

Our business strategy includes the entry into additional collaborative agreements. We may not be able to enter into additional collaborative agreements or may not be able to negotiate commercially acceptable terms for these agreements

Our current business strategy includes the entry into additional collaborative agreements for the development and commercialization of our pharmaceutical product candidates, including, but not limited to DUR-928, ORADUR-Methylphenidate ER in markets not already licensed to Orient Pharma, including the United States and Europe, and others. The negotiation and consummation of these types of agreements typically involve simultaneous discussions with multiple potential collaborators and require significant time and resources from our officers, business development, legal, and research and development staff. In addition, in attracting the attention of pharmaceutical and biotechnology company collaborators, we compete with numerous other third parties with product opportunities as well as the collaborators' own internal product opportunities. We may not be able to consummate additional collaborative agreements, or we may not be able to negotiate commercially acceptable terms for these agreements. If we do not consummate additional collaborative agreements, we may have to consume money more rapidly on our product development efforts, defer development activities or forego the exploitation of certain geographic territories, any of which could have a material adverse effect on our business.

We and our third-party collaborators may not be able to manufacture sufficient quantities of our pharmaceutical product candidates and components to support the non-clinical, clinical and commercial requirements of our collaborators and ourselves at an acceptable cost or in compliance with applicable government regulations, and we have limited manufacturing experience

We or our third-party collaborators to whom we have assigned such responsibility must manufacture our pharmaceutical product candidates and components in non-clinical, clinical and commercial quantities, either directly or through third parties, in compliance with regulatory requirements and at an acceptable cost. The manufacturing processes associated with our product candidates are complex. We and our third-party collaborators, where relevant, have not yet completed development of the manufacturing process for any product candidates or components, including DUR-928, REMOXY ER and POSIMIR. If we and our third-party collaborators, where relevant, fail to timely complete the development of the manufacturing process for our product candidates, we and our third-party collaborators, where relevant, will not be able to timely produce product for non-clinical, clinical trials and commercialization of our product candidates. We have also committed to manufacture and supply product candidates or components under a number of our

collaborative agreements with third-party companies. We have limited experience manufacturing pharmaceutical products, and we may not be able to timely accomplish these tasks. If we and our third-party collaborators, where relevant, fail to develop manufacturing processes to permit us to manufacture a product candidate or component at an acceptable quality and cost, then we and our third-party collaborators may not be able to develop or commercialize that product candidate or we may be in breach of our supply obligations to our third-party collaborators.

Our manufacturing facility in Cupertino is a multi-disciplinary site that we have used to manufacture only research and clinical supplies of several of our pharmaceutical product candidates, including POSIMIR and REMOXY ER. If we experience delays or technical difficulties in developing acceptable manufacturing processes or scaling up the manufacturing of our product candidates, it could result in delays or added cost in our development programs. We have not manufactured commercial quantities of any of our product candidates. In the future, we intend to develop additional manufacturing capabilities for our product candidates and components to meet our demands and those of our third-party collaborators by contracting with third-party manufacturers and by potentially constructing additional manufacturing space at our facilities in California and Alabama. We have limited experience building and validating manufacturing facilities, and we may not be able to accomplish these tasks in a timely or cost effective manner.

If we and our third-party collaborators, where relevant, are unable to manufacture our pharmaceutical product candidates or components in a timely manner or at an acceptable cost, quality or performance level, and are unable to attain and maintain compliance with applicable regulations, the non-clinical and clinical trials and the commercial sale of our product candidates and those of our third-party collaborators could be delayed. Additionally, we may need to alter our facility design or manufacturing processes, install additional equipment or do additional construction or testing in order to meet regulatory requirements, optimize the production process, increase efficiencies or production capacity or for other reasons, which may result in additional cost to us or delay production of product needed for the non-clinical trials, clinical trials, chemistry, manufacturing and controls (CMC) and commercial launch of our product candidates and those of our third-party collaborators.

We have entered into a commercial manufacturing and packaging agreement with a third party manufacturer for future supply of POSIMIR. This third party is our sole source for the drug product required for development and commercialization of this drug candidate. There may be technical risks associated with establishing an alternative commercial manufacturer that could entail delays in supply, quality issues or delays in the possible regulatory approval of POSIMIR. Furthermore, we and our contract manufacturer may also need or choose to subcontract with additional third-party contractors to perform manufacturing steps of POSIMIR or supply required components for POSIMIR. Where third party contractors perform manufacturing services for us, we will be subject to the schedule, expertise and performance of third parties as well as incur significant additional costs. Failure of third parties to perform their obligations could adversely affect our operations, development timeline and financial results. If we proceed with the development of POSIMIR, we expect to put in place in the future second source supply arrangements, which may be costly and time consuming.

We have entered into contract manufacturing agreements with multiple vendors for DUR-928. There can be no assurance that we will receive sufficient quantities of DUR-928 to commence and conduct the non-clinical trials, clinical trials and CMC activities we are planning, and delays in supply could delay development of DUR-928.

If we or our third-party collaborators cannot manufacture our pharmaceutical product candidates or components in time to meet the clinical or commercial requirements of our collaborators or ourselves or at an acceptable cost, our operating results will be harmed.

Failure to comply with ongoing governmental regulations for our pharmaceutical product candidates could materially harm our business in the future

Developing, manufacturing, marketing or promoting a drug is subject to very strict controls. Furthermore, clearance or approval may entail ongoing requirements for post-marketing studies. 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 use of our 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 GMP, GLP and/or other governmental requirements for drug development;
- failure to obtain approvals for clinically intended uses of our pharmaceutical product candidates under development; or
- FDA required product withdrawals or warnings arising from identification of serious and unanticipated adverse side effects in our product candidates.

Manufacturers of drugs must comply with the applicable FDA good manufacturing practice 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 good manufacturing practices regulations is difficult and costly. Manufacturing facilities are subject to ongoing periodic inspection by the FDA and corresponding state agencies, including unannounced inspections, and must be licensed before they can be used for the commercial manufacture of our development products. We and/or our present or future suppliers and distributors may be unable to comply with the applicable good manufacturing practice regulations and other FDA regulatory requirements. We have not been subject to a good manufacturing practice regulation inspection by the FDA relating to our product candidates. If we, our third-party collaborators or our respective suppliers do not achieve compliance for our product candidates we or they manufacture, the FDA may refuse or withdraw marketing clearance, put our or our partner's clinical trial on hold, withdraw or reject an investigational new drug (IND) application or require product recall, which may cause interruptions or delays in the development, manufacture and sale of our product candidates.

We have a history of operating losses, expect to continue to have losses in the future and may never achieve or maintain profitability

We have incurred significant operating losses since our inception in 1998 and, as of September 30, 2018, had an accumulated deficit of approximately $461.3 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, and manufacture and market our proposed product candidates. Development of pharmaceutical product candidates is costly and requires significant investment. In addition, we may choose to license from third parties either additional drug delivery platform technology or rights to particular drugs or other appropriate technology and/or intellectual property rights for use in our product candidates. The license fees for these technologies or rights would increase the costs of our product candidates.

To date, we have not generated significant revenue from the commercial sale of our pharmaceutical product candidates and do not expect to do so in the near future. Our current revenues are from the ALZET product line, from the LACTEL product line and from certain excipient sales, and from payments under collaborative research and development agreements with third parties. We do not expect our product revenues to increase significantly in the near future, and we do not expect that collaborative research and development revenues will exceed our actual operating expenses. We do not anticipate meaningful revenues to derive from the commercialization and marketing of our product candidates in development in the near future, and therefore do not expect to generate sufficient revenues to cover expenses or achieve profitability in the near future.

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

We have a small sales and marketing group focused on our ALZET and LACTEL product lines. We may choose to develop our own sales force and commercial group to market 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 personnel. If we are not able to put in place an appropriate sales force and commercial group for our products in development, we may not be able to effectively launch these products. We may not be able to effectively sell our 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 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, if relevant, may be unable to establish a sufficient sales and marketing organization on a timely basis, if at all. We and our third-party collaborators, if relevant, may be unable to engage qualified distributors. Even if engaged, these distributors may:

- fail to satisfy financial or contractual obligations to us;
- fail to adequately market our product candidates;
- cease operations 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 product candidates; or
- build up inventory in excess of demand thereby limiting future purchases of our 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 product candidates will hurt our business, prospects and financial results.

We rely heavily on third parties to support development, clinical testing and manufacturing of our product candidates

We rely on third-party contract research organizations, consultants, service providers and suppliers to provide critical services to support development, clinical testing, and manufacturing of our product candidates. For example, we currently depend on third-party vendors to manage and monitor our clinical trials and to perform critical manufacturing steps for our product candidates. These third parties may not execute their responsibilities and tasks competently in compliance with applicable laws and regulations or in a timely fashion. We rely on third-parties to manufacture or perform manufacturing steps relating to our product candidates or 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 product candidates. 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 development products, increase our expenses and materially harm our business, financial condition and results of operations.

Key components of our product candidates are provided by limited numbers of suppliers, and supply shortages or loss of these suppliers could result in interruptions in supply or increased costs

Certain components and drug substances used in our and our collaborators' product candidates, including DUR-928, POSIMIR, Methydur, PERSERIS and REMOXY ER, are currently purchased from a single or a limited number of outside sources. In particular, Eastman Chemical is the sole supplier, pursuant to a supply agreement entered into in December 2005, of our requirements of sucrose acetate isobutyrate, a necessary component of POSIMIR, REMOXY ER, ORADUR-Methylphenidate and certain other pharmaceutical product candidates we have under development, and a third party manufacturer is our sole supplier for future clinical and commercial supplies of POSIMIR. The reliance on a sole or limited number of suppliers could result in:

- delays associated with redesigning a pharmaceutical product candidate due to a failure to obtain a single source component;
- 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 technology to the new supplier;
- an inability to obtain an adequate supply of required components; and
- reduced control over pricing, quality and delivery time.

We have supply agreements in place for certain components of our pharmaceutical product candidates, but do not have in place long term supply agreements with respect to all of the components of any of our product candidates. Therefore the supply of a particular component could be terminated 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 quantity, quality and cost acceptable to us. Any interruption in the supply of single source components could cause us to seek alternative sources of supply or manufacture these components internally. 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 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 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.

If we are unable to adequately protect, maintain or enforce our intellectual property rights or secure rights to third-party patents, we may lose valuable assets, experience reduced market share or incur costly litigation to protect our rights 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 2, 2018, we owned or exclusively in-licensed over 50 unexpired issued U.S. patents and over 305 unexpired issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have over 35 pending U.S. patent applications and over 90 foreign applications pending in Europe, Australia, Japan, Canada and other countries.

The patent status of our most advanced drug candidates is as follows:

Our Epigenetic Regulator Program includes ten in-licensed patent families and one patent family solely owned by us. Two patent families each include two granted patents expiring in at least 2026 and 2032, respectively. The other patent families include pending patent applications, which if granted, could result in patents expiring in 2033, 2034, 2035, 2037, 2037, 2037, 2040 and 2040,

respectively, plus any eligible patent term adjustments and extensions. Of the eleven patent families covering DUR-928 and/or other molecules in the Epigenetic Regulator Program, two were only filed in the United States, and the other nine have been filed or likely will be filed both in the U.S. and internationally. Since DUR-928 is an endogenous small molecule, patent claims directed to DUR-928 composition of matter may be more difficult to maintain or enforce in the United States under *Myriad Genetics* and other recent court decisions. One of the U.S. patents issued before *Myriad Genetics*, and three of the DUR-928 U.S. patents issued after *Myriad Genetics*. The granted claims in the U.S. include both composition of matter and method of treatment claims. 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 would result in the loss of our rights to these patent families.

In the United States, POSIMIR is covered by two patent families. One patent family includes granted patents expiring in at least 2025. Another patent family includes a pending patent application, which if granted, could result in a patent expiring in 2026, plus any eligible patent term adjustments and extensions. In Europe, POSIMIR is covered by five granted patents with three expiring in 2025 and two expiring in 2026, plus any eligible patent term extensions.

In the United States, our REMOXY ER patent portfolio includes four patent families. Three patent families include granted patents expiring in at least 2025, 2031, and 2034, respectively. The patent family providing protection until at least 2025 includes twelve granted patents. The patent family providing protection until at least 2031 includes two granted patents. The patent family providing protection until at least 2034 includes four granted patents. The fourth patent family includes a pending patent application, which if granted, could result in a patent expiring in 2026, plus any eligible patent term adjustments and extensions. We currently have pending U.S. applications for each of these four patent families. There can be no assurance that the pending patent applications will be granted. In Europe, REMOXY ER is covered by five granted patents with two expiring in 2023, two expiring in 2026, and one expiring in 2028, plus any eligible patent term extensions.

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.

The patent laws of the United States have recently undergone changes through court decisions which may have significant impact on us and our industry. Decisions of the U.S. Supreme Court and other courts with respect to the standards of patentability, constitutionality of inter partes reviews, enforceability, availability of injunctive relief and damages may make it more difficult for us to procure, maintain, defend and enforce patents. In addition, the America Invents Act was signed into law in September 2011, which among other changes to the U.S. patent laws, changed patent priority from "first to invent" to "first to file," implemented a post-grant opposition system for patents and provided a prior user defense to infringement. These judicial and legislative changes have introduced significant uncertainty in the patent law landscape and may potentially negatively impact our ability to procure, maintain and enforce patents to provide exclusivity for our products.

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 appropriate 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.

Our collaboration agreements may depend on our intellectual property

We are party to collaborative agreements with Sandoz, Pain Therapeutics, Orient Pharma and Santen 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 dispute which we would otherwise spend on our business. To the extent that our agreements call for future royalties to be paid conditional on our having patents covering the royalty-bearing subject matter, the decision by the Supreme Court in the case of *MedImmune v. Genentech* and other caselaw could encourage our licensees to challenge the validity of our patents and thereby seek to avoid future royalty obligations without losing the benefit of their license. Should they be successful in such a challenge, our ability to collect future royalties could be substantially diminished.

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

We or our collaborators may be exposed to future litigation by third parties based on claims that our 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 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. We also may not have sufficient funds to litigate 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 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 pharmaceutical product candidates that incorporate the challenged intellectual property, which would adversely affect our revenue;
- 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 product candidates, which would be costly and time-consuming.

Technologies and businesses which we acquire or license may be difficult to integrate, disrupt our business, dilute stockholder value or divert management attention

We may acquire technologies, products or businesses to broaden the scope of our existing and planned product lines and technologies. Future acquisitions expose us to:

- increased costs associated with the acquisition and operation of the new businesses or technologies and the management of geographically dispersed operations;
- the risks associated with the assimilation of new technologies, operations, sites and personnel;
- the diversion of resources from our existing business and technologies;
- the inability to generate revenues to offset associated acquisition costs;
- the requirement to maintain uniform standards, controls, and procedures; and
- the impairment of relationships with employees and customers or third party collaborators as a result of any integration of new management personnel.

Acquisitions may also result in the issuance of dilutive equity securities, the incurrence or assumption of debt or liabilities or additional expenses associated with the amortization of acquired intangible assets or potential businesses. Acquisitions may not generate any additional revenue or provide any benefit to our business.

Some of our pharmaceutical product candidates contain controlled substances, the making, use, sale, importation, exportation and distribution of which are subject to regulation by state, federal and foreign law enforcement and other regulatory agencies

Some of our product candidates currently under development contain, and our products in the future may contain, controlled substances which are subject to state, federal and foreign laws and regulations regarding their manufacture, use, sale, importation and distribution. REMOXY ER, and certain other product candidates we may develop contain active ingredients which are classified as controlled substances under the regulations of the U.S. Drug Enforcement Agency. For our product candidates containing controlled substances, we and our suppliers, manufacturers, contractors, customers and distributors are required to obtain and maintain applicable

registrations from state, federal and foreign law enforcement and regulatory agencies and comply with state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation and distribution of controlled substances. These regulations are extensive and include regulations governing manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, record keeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of drug candidates including controlled substances. Failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidates containing controlled substances and subject us to enforcement action. In addition, because of their restrictive nature, these regulations could limit our commercialization of our product candidates containing controlled substances. In particular, among other things, there is a risk that these regulations may interfere with the supply of the drugs used in our clinical trials, and in the future, our ability to produce and distribute our products in the volume needed to meet commercial demand.

Write-offs related to the impairment of our goodwill, long-lived assets, inventories and other non-cash charges, as well as stock-based compensation expenses may adversely impact or delay our profitability

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 $6.4 million at September 30, 2018. 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 2017 and determined that goodwill was not impaired as of December 31, 2017. 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 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. In addition, these circumstances may cause us to record a liability related to minimum purchase agreements that we have in place for raw materials. For example, we recorded charges to cost of goods sold of approximately $926,000, of which approximately $426,000 related to the write-down of the cost basis of inventory and approximately $500,000 related to the prepaid inventory for the minimum purchase commitment for an excipient in the year ended December 31, 2016 as a result of a change in the forecasted demand for the excipients after Pain Therapeutics received a Complete Response Letter from the FDA on its resubmission of the NDA for REMOXY ER. In addition, during the year ended December 31, 2017, we recorded charges to cost of goods sold of approximately $2.0 million, of which approximately $503,000 related to the write-down of the cost basis of inventory on hand, $500,000 related to the prepaid inventory for the minimum purchase commitment for the excipient, and $1.0 million related to the recognition of our remaining minimum purchase commitment for the same excipient after we announced that PERSIST, the Phase 3 clinical trial for POSIMIR, did not meet its primary efficacy endpoint.

Global credit and financial market conditions could negatively impact the value of our current portfolio of cash equivalents, short-term investments or long-term investments and our ability to meet our financing objectives

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 in 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, 2018, 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 need to hire additional qualified personnel

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. 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. 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.

We may not successfully manage our company through varying business cycles

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. To manage through such cycles, we must expand or contract our facilities, our operational, financial and management systems and our personnel. If we were unable to manage growth and contractions effectively our business would be harmed.

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 and pharmaceutical 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 involve the use, generation and disposal of hazardous materials, including but not limited to certain hazardous chemicals, solvents, agents and biohazardous materials. The extent of our use, generation and disposal of such substances has increased substantially since we started manufacturing and selling biodegradable polymers. 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.

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 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 geographical area that is seismically active and 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. Should such a natural disaster 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 destroyed.

Risks Related To Our Industry

The market for our pharmaceutical product candidates and ALZET and LACTEL product lines is rapidly changing and competitive, and new products or technologies developed by others could impair our ability to 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 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 DUR-928, if approved, will depend on the specific indications for which DUR-928 is approved. Intercept, Gilead, Shire, Conatus Pharmaceuticals, Galectin Therapeutics, Genfit, Pfizer, Roche, Bristol Myers Squibb, Novartis, Terns Pharmaceuticals, Galmed Pharmaceuticals, Enanta Pharmaceuticals, Novo Nordisk, Takeda, Vital Therapies, Allergan, Akarna Therapeutics, Inventiva Pharma, Genkyotex, VBL Therapeutics, NGM Biopharmaceuticals, Gemphire Therapeutics, Albireo Pharma, CymaBay Therapeutics, Madrigal Pharmaceuticals, Viking Therapeutics, CohBar, FALK Pharma, Acorda, and others have development plans for products to treat NAFLD/NASH, PSC or other liver diseases. AbbVie, Ischemix, Thrasos Therapeutics, AM-Pharma, Complexa, Quark Pharmaceuticals and others have development plans for products to treat acute kidney injury. Bristol Myers Squibb, Novartis, Eli Lilly, Almirall, LEO Pharma, Pfizer, Janssen, AbbVie, Boerhinger-Ingelheim, Amgen, Sandoz, Astra-Zeneca, Valeant, Takeda, Merck, Idera Pharmaceuticals and others have development plans for products to treat psoriasis.

POSIMIR and REMOXY ER, if approved, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, implantable and external infusion pumps which can be used for infusion of opioids and local anesthetics. Products of these types are marketed by Purdue Pharma, AbbVie, Janssen, Actavis, Medtronic, Endo, AstraZeneca, Pernix Therapeutics, Tricumed, Halyard Health, Cumberland Pharmaceuticals, Pacira, Acorda Therapeutics, Mallinckrodt, Inspirion Delivery Technologies, Mylan, Shire, Johnson & Johnson, Eli Lilly, Pfizer, Novartis, Egalet, Teva Pharmaceuticals, Collegium Pharmaceutical and others. Purdue Pharma, Sandoz, Actavis, Collegium Pharmaceutical, Pfizer, Elite Pharmaceuticals, Intellipharmaceutics, Egalet, Teva Pharmaceuticals and others have also announced regulatory approval or development plans for abuse deterrent opioid products. PERSERIS will compete with currently marketed or approved products by Johnson & Johnson, Eli Lilly, Otsuka, Alkermes, Merck, Allergan, Novartis, and others. Our ORADUR-ADHD product candidates, if approved, will compete with currently marketed or approved products by Shire, Johnson & Johnson, UCB, Novartis, Noven, Eli Lilly, Pfizer and others.

Numerous companies are applying significant resources and expertise to the problems of drug delivery and several of these are focusing or may focus on delivery of drugs to the intended site of action, including Alkermes, Pacira, Immune Pharmaceuticals, Innocoll, Nektar, Kimberly-Clark, Acorda Therapeutics, Flamel, Alexza, Mallinckrodt, Hospira, Pfizer, Cumberland Pharmaceuticals, Egalet, Acura, Elite Pharmaceuticals, Phosphagenics, Intellipharmaceutics, Collegium Pharmaceutical, Heron Therapeutics, Charleston Laboratories, Daiichi Sankyo and others. Some of these competitors may be addressing the same therapeutic areas or indications as we are. Our current and potential competitors may succeed in obtaining patent protection or commercializing products before us. Many of these entities have significantly greater research and development capabilities than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors' financial, marketing, manufacturing and other resources.

Competition for our ALZET product line primarily consists of customers choosing to utilize delivery methods for their research projects other than an osmotic pump. Competition for our LACTEL product line comes from companies including Evonik, Corbion, FUJIFILM Wako Pure Chemical Corporation, PCAS and others. Many of these entities have significantly greater research and development capabilities than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. We may in the future face competition for our ALZET and LACTEL product lines 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 product candidates. Our competitors may develop products that are safer, more effective or less costly than our product candidates and, therefore, present a serious competitive threat to our product offerings.

The widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our product candidates even if commercialized. Chronic and post-operative pain are currently being treated by oral medication, transdermal drug delivery systems,

such as drug patches, injectable products and implantable drug delivery devices which will be competitive with our product candidates. 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 product candidates to receive widespread acceptance if commercialized.

Our relationships with customers and third-party payers will be subject to applicable anti-kickback, fraud and abuse 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 any product candidates for which we obtain marketing approval. Our future arrangements with third-party payers and customers may expose us 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 would 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; and
- 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, and state and foreign laws governing the privacy and security of health information in specified circumstances, 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will 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 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 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 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 has continued 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. Among the provisions of the Affordable Care Act of importance to us are the following:

- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" and biologic agents;
- imposes an annual excise tax of 2.3% on any entity that manufactures or imports medical devices offered for sale in the United States;
- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- addresses new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extension products;
- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extends manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- mandates a further shift in the burden of Medicaid payments to the states;
- expands the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- establishes a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- establishes a new Patient Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishes an independent payment advisory board that will submit recommendations to Congress to reduce Medicare spending if projected Medicare spending exceeds a specified growth rate.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future. The new Presidential Administration and U.S. Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act. It is uncertain the extent to which any such changes may impact our business or financial condition.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include the Budget Control Act of 2011, which, among other things, resulted in reductions to Medicare payments to providers of 2% per fiscal year and will remain in effect through 2025; 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; and the Medicare Access and CHIP Reauthorization Act of 2015, which, among other things, ended the use of the sustainable growth rate formula and provides for a 0.5% update to physician payment rates for each calendar year through 2019, after which there will be a 0% annual update each year through 2025. 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 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.

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 new law, to become effective in January 2019, which will require 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 are slow or unable to adapt to new requirements or policies, or if we are not able to maintain regulatory compliance, our products and product candidates may lose any regulatory approval that may have been obtained and we may not 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 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 product candidates, our present product liability insurance may be inadequate and may not fully cover the costs of any claim or any ultimate damages we might be required to pay. Product liability claims or other claims related to our 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 product candidates. A product liability claim could also significantly harm our reputation and delay market acceptance of our product candidates.

Acceptance of our pharmaceutical product candidates in the marketplace 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 in research and development, including DUR-928, and POSIMIR, if approved, and including Indivior's PERSERIS. Even if approved for marketing, our product candidates may not achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including:

- the receipt of regulatory clearance of marketing claims for the uses that we are developing;
- the establishment and demonstration in the medical community of the safety and clinical efficacy of our products and their potential advantages over existing therapeutic products; and
- pricing and reimbursement policies of government and third-party payors such as insurance companies, health maintenance organizations, hospital formularies and other health plan administrators.

In addition, market adoption of POSIMIR and other products in development may depend on what data from clinical studies is included in the product label, and there can be no assurance as to what the final product labels will contain. Physicians, patients, payers or the medical community in general may be unwilling to accept, utilize or recommend any of our products. If we are unable to obtain regulatory approval, commercialize and market our future products when planned and achieve market acceptance, we will not achieve anticipated revenues.

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

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 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 product candidates will depend in part on the extent to which appropriate reimbursement levels for the cost of our product candidates and related treatment are obtained by governmental authorities, private health insurers and other organizations, such as HMOs. Third-party payers often limit payments 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 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.

If we or our third-party collaborators are unable to train physicians to use our pharmaceutical product candidates to treat patients' diseases or medical conditions, we may incur delays in market acceptance of our products

Broad use of our product candidates will require extensive training of numerous physicians on the proper and safe use of our product candidates. The time required to begin and complete training of physicians could delay introduction of our products and adversely affect market acceptance of our products. We or third parties selling our product candidates may be unable to rapidly train physicians in numbers sufficient to generate adequate demand for our product candidates. Any delay in training would materially delay the demand for our product candidates and harm our business and financial results. In addition, we 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, 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 revenue-generating activities to compliance activities.

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 has 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 has also initiated or is considering 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 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 and results of operations.

Risks Related To Our Common Stock

Our stock price has in the past and may in the future 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

On each of January 16, 2013 and December 9, 2014, we received written notification from Nasdaq informing us that because the closing bid price of our common stock was below $1.00 for 30 consecutive trading days, our shares no longer complied with the minimum closing bid price requirement for continued listing on the Nasdaq Global Market under Nasdaq Marketplace Rule 5450(a)(1). Each time, we were given a period of 180 days from the date of the notification to regain compliance with Nasdaq's listing requirements by having the closing bid price of our common stock listed on Nasdaq be at least $1.00 for at least 10 consecutive trading days.

While we regained compliance within the applicable time periods as of February 1, 2013 and March 6, 2015, respectively, if our shares again no longer comply with the minimum closing bid price requirement for continued listing on the Nasdaq Global Market under Nasdaq Marketplace Rule 5450(a)(1) and we do not regain compliance within the applicable 180-day time period, we may transfer our common stock listing to The Nasdaq Capital Market, provided that the Company (i) meets the applicable market value of publicly held shares requirement for continued listing and all other applicable requirements for initial listing on The Nasdaq Capital Market (except for the closing bid price requirement) based on the Company's most recent public filings and market information and (ii) notifies Nasdaq of its intent to cure this deficiency. Following a transfer to The Nasdaq Capital Market, the Company would be afforded the remainder of an additional 180 calendar day grace period in order to regain compliance with the minimum closing bid price requirement of $1.00 per share under The Nasdaq Capital Market, unless it does not appear to Nasdaq that it would be possible for the Company to cure the deficiency.

If compliance is not demonstrated within the applicable compliance period, Nasdaq will notify the Company that its securities will be subject to delisting. The Company may appeal Nasdaq's determination to delist its securities to a Hearings Panel. During any appeal process, shares of the Company's common stock would continue to trade on the Nasdaq Global Market or Nasdaq Capital Market, as applicable.

There can be no assurance that we will maintain compliance with the requirements for listing our common stock on the Nasdaq Global Market or if we were not in compliance, that our common stock would be eligible for transfer to the Nasdaq Capital Market and remain in compliance with the requirements for listing on that market. 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 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 financing 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.

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 no approved pharmaceutical products, particularly companies in new and rapidly evolving markets such as pharmaceuticals, drug delivery 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 may require additional funds to complete the development of our 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 August 2018, we filed a shelf registration statement on Form S-3 with the SEC that allows us to offer up to $175 million of securities from time to time in one or more public offerings, inclusive of up to $75.0 million of additional shares of common stock which the Company may sell, subject to

certain limitations, under the 2015 Sales Agreement through Cantor Fitzgerald, acting as agent. Any additional sales in the public market of our common stock, under our Controlled Equity Offering program with Cantor Fitzgerald, in other offerings under the shelf registration statement or otherwise, could adversely affect prevailing market prices for our common stock. In addition, as of September 30, 2018, 30,970,551 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 $1.63 per share and 8,604,997 additional shares of common stock reserved for potential future issuance under our stock option plan, and an aggregate of 419,251 shares of common stock reserved for potential future issuance under our 2000 Employee Stock Purchase Plan. Investors will incur dilution from the sale of any additional shares or upon the issuance of any shares pursuant to such plans, or upon exercise of any outstanding options.

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:

- failure of third-party collaborators to continue development of the respective product candidates they are developing;
- adverse results (including adverse events or failure to demonstrate safety or efficacy) or delays in our clinical and non-clinical trials of DUR-928 or other product candidates;
- announcements of FDA non-approval of our product candidates, 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 product candidates, clinical trials, manufacturing processes or sales and marketing activities, or those of our third party collaborators;
- announcements of technological innovations, patents, product approvals or new products by our competitors;
- regulatory, judicial and patent developments in the United States and foreign countries;
- any lawsuit involving us or our 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;
- actual or anticipated variations in our operating results;
- changes in recommendations by securities analysts or lack of analyst coverage;
- negative press coverage or online mis-information 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 Global Market;
- loss or disruption of facilities due to natural disasters;
- 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 recently experienced extreme price and volume 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 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 used and may from time to time invest in ways with which our stockholders may not agree and that do not yield favorable returns.

Executive officers, directors and principal stockholders have substantial control over us, which could delay or prevent a change in our corporate control favored by our other stockholders

Our directors, executive officers and principal stockholders, together with their affiliates, have substantial control over us. The interests of these stockholders may differ from the interests of other stockholders. As a result, these stockholders, if acting together, could have the ability to exercise control over all corporate actions requiring stockholder approval irrespective of how our other stockholders may vote, including:

- the election of directors;
- the amendment of charter documents;
- the approval of certain mergers and other significant corporate transactions, including a sale of substantially all of our assets; or
- the defeat of any non-negotiated takeover attempt that might otherwise benefit the public stockholders.

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 2. Unregistered Sales of Equity Securities and Use of Proceeds

None

Item 3. Defaults Upon Senior Securities

None

Item 4. Mine Safety Disclosures

Not applicable

Item 5. Other Information

None

Item 6. Exhibits

Exhibit Number	Exhibit Name
10.1	Fifth Amendment to Lease between De Anza Enterprises and the Company dated as of August 15, 2018 ((incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on August 17, 2018).
10.2	Third Amendment to Lease between Handley Management Corporation, as successor-by-merger to Renault & Handley Employee Investments Co. and the Company dated September 17, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on September 21, 2018).
10.3*	Exclusive License Agreement between the Company and Virginia Commonwealth University Intellectual Property Foundation dated December 5, 2012.
10.4*+	Amendment No. 1 to Exclusive License Agreement between the Company and Virginia Commonwealth University Intellectual Property Foundation dated July 2, 2015.
10.5*+	Amendment No. 2 to Exclusive License Agreement between the Company and Virginia Commonwealth University Intellectual Property Foundation dated March 6, 2018.
31.1*	Rule 13a-14(a) Section 302 Certification of James E. Brown.
31.2*	Rule 13a-14(a) Section 302 Certification of Michael H. Arenberg.
32.1*	Certificate pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 of James E. Brown.
32.2*	Certificate pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 of Michael H. Arenberg.
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.
+ Confidential treatment requested with respect to certain portions of this exhibit.

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 8, 2018

By: /S/ MICHAEL H. ARENBERG
Michael H. Arenberg
Chief Financial Officer and Principal Accounting Officer

Date: November 8, 2018

Exhibit 10.3

EXCLUSIVE LICENSE AGREEMENT

THIS EXCLUSIVE LICENSE AGREEMENT is made and entered into this 5th day of December, 2012, by and between: **DURECT CORPORATION,** a Delaware corporation (hereinafter referred to as the "LICENSEE") with its principal place of business at 10260 Bubb Road, Cupertino, CA 95014, and **VIRGINIA COMMONWEALTH UNIVERSITY INTELLECTUAL PROPERTY FOUNDATION** (hereinafter referred to as the "LICENSOR"), and with its principal place of operation at Virginia Commonwealth University, 800 E. Leigh Street, Suite 3000, Richmond, Virginia 23298-0568.

WHEREAS, LICENSOR is charged with management and licensing of intellectual properties developed at Virginia Commonwealth University ("VCU") and, under VCU intellectual property policy, inventions made by employees of VCU or made using the facilities of VCU are required to be assigned to VCU and managed by LICENSOR;

WHEREAS, VCU and/or the United States Department of Veterans Affairs (hereinafter called "VA") are joint or sole owners of all right, title, and interest in patent applications and inventions and know-how associated with the VCU Invention Disclosures as listed in Appendix A attached hereto and made a part hereof, and other LICENSED TECHNOLOGY (defined herein).

WHEREAS, LICENSOR and the VA are parties to an Inter-Institutional Agreement (the "IIA" attached as Appendix C) dated August 7, 2002 which provides that LICENSOR is authorized to (a) negotiate, execute and administer license agreements granting rights to LICENSED PATENT RIGHTS (defined herein) on behalf of VA and (b) receive on behalf of VA amounts paid in consideration of such grant of rights and to share a portion of such amounts with VA;

WHEREAS, LICENSOR and LICENSEE entered into an Option Agreement on December 8, 2011 (hereinafter "Option Agreement") and an Amendment to the Option Agreement effective April 19, 2012, and LICENSEE has exercised its right to license LICENSED TECHNOLOGY and LICENSED PATENT RIGHTS;

WHEREAS, among other things, this Agreement is intended to implement the binding terms set forth in the Term Sheet Appendix to Option Agreement signed by the parties and dated April 19, 2012;

WHEREAS LICENSEE is desirous of acquiring from LICENSOR certain rights set forth below and LICENSOR wishes to grant licenses to such rights to LICENSEE as set forth herein;

NOW, THEREFORE, in consideration of the promises and the covenants set forth herein, LICENSOR and LICENSEE agree as follows:

I. DEFINITIONS

The following definitions shall apply in the interpretation of this Agreement.

1.1 "AFFILIATE" of any company means any corporation which, directly or indirectly, controls or is controlled by, or is under direct or indirect common control with, such company; and for the purposes of this definition "control" (including "control by" and "under common control with") as used with respect to any corporation or company, shall mean the possession, directly or indirectly, of the power to direct or cause the direction of the management and policies of such corporation or company, through the ownership of more than 50% of the voting shares.

1.2 “CALENDAR QUARTER” means the three-month period ending March 31, June 30, September 30, or December 31 in any year.

1.3 “CDA” shall have the meaning ascribed to such term in Section 9.12.

1.4 “COLLABORATION IMPROVEMENTS” means IMPROVEMENTS not falling under the SRA TECHNOLOGY, that are developed, generated, made, conceived or reduced to practice jointly by or on behalf of INVENTOR(S) and NON-INVENTOR(S).

1.5 “COMMERCIALLY REASONABLE EFFORTS” shall mean those efforts and resources consistent with such efforts used by similarly situated pharmaceutical companies in developing products having similar development and regulatory risks (including the likelihood of regulatory approval given the regulatory framework involved), costs and efforts, as well as similar patent protection and commercial (including profit) potential in view of, among other things, the competitive landscape. COMMERCIALLY REASONABLE EFFORTS shall be determined on a country-by-country or market-by-market basis (as most applicable) for a LICENSED PRODUCT.

1.6 “Dual Appointment Personnel or DAP” shall mean any person who is employed by both VCU and VA, or has signed a VA-WOC Appointee Intellectual Property Agreement as defined in the IIA.

1.7 “EFFECTIVE DATE” shall mean the date of the Agreement set forth above.

1.8 “FIELD OF USE” shall mean all fields of use.

1.9 “Force Majeure” shall have the meaning ascribed to such term in Section 9.9.

1.10 “IMPROVEMENT(S)” means any and all enhancements of, modifications to, improvements on or developments (including, in each case, any inventions or discoveries) relating to any of the LICENSED TECHNOLOGY, that are developed, generated, made, conceived or reduced to practice at least in part by or on behalf of VCU (including any University Employees as defined in the IIA) and/or DAP personnel (collectively, “VCU/VA Personnel”) during the course of research conducted by them as of the EFFECTIVE DATE and during the term hereof, including SRA TECHNOLOGY (defined herein) and, with respect to any and all of the foregoing, intellectual property rights therein and thereto including any and all United States and foreign patents and patent applications disclosing, covering or claiming any such enhancements, modifications, improvements or developments (including, in each case, any inventions or discoveries), and any United States (and foreign equivalents of) extensions, substitutions, continuations, confirmations, divisions, reissues, reexaminations, restorations, registrations and continuation-in-part applications that are entitled to the priority date of any such applications, with respect to any or all of the foregoing, and enforcement rights. Improvements made solely by VA Personnel that are not governed by IIA shall not be considered IMPROVEMENTS under this Agreement.

1.11 “Indemnitees” shall have the meaning ascribed to such term in Section 9.5.

1.12 “INVENTOR(S) means Dr. Shunlin Ren, Dr. William Pandak, and/or other VCU/VA Personnel who are under Dr. Ren’s supervision, or working in a laboratory managed or controlled by Dr. Ren or Dr. Pandak.

1.13 “INVENTOR IMPROVEMENT(S)” means IMPROVEMENTS not falling under the SRA TECHNOLOGY, that are developed, generated, made, conceived or reduced to practice solely by or on behalf of INVENTOR(S).

1.14 ”Joint Patents” shall have the meaning ascribed to such term in Section 8.2.

1.15 “Liabilities” shall have the meaning ascribed to such term in Section 9.5.

1.16 “LICENSED PATENT RIGHTS” shall mean (a) those patent applications listed in Appendix A and patents issuing therefrom, any foreign equivalents thereof, and any and all United States (and foreign equivalents of) extensions, substitutions, continuations, confirmations, divisions, reissues, reexaminations, restorations, registrations and continuation-in-part applications that are entitled to the priority date of any such applications, with respect to any or all of the foregoing, in each case as of the EFFECTIVE DATE and thereafter that are filed or issued during the term of this Agreement, and enforcement rights; (b) those United States and foreign patent applications and patents disclosing, covering or claiming any LICENSED TECHNOLOGY and, in each case, any and all United States (and foreign equivalents of) extensions, substitutions, continuations, confirmations, divisions, reissues, reexaminations, restorations, registrations and continuation-in-part applications that are entitled to the priority date of any such applications, with respect to any or all of the foregoing, that are filed or issued during the term of this Agreement, and enforcement rights.

1.17 “LICENSED PRODUCTS” shall mean any product or process in the FIELD OF USE embodying LICENSED TECHNOLOGY or that incorporates, is covered, disclosed or claimed by, or is made, in whole or part, by the use of the LICENSED PATENT RIGHTS.

1.18 “LICENSED TECHNOLOGY” shall mean and include:

(i) the technologies, inventions and know-how associated with the VCU Invention Disclosures listed in Appendix A,

(ii) SRA TECHNOLOGY, INVENTOR IMPROVEMENT(S), COLLABORATION IMPROVEMENTS and any NON-INVENTOR IMPROVEMENT(S) that LICENSEE elects to add to this AGREEMENT under Section 2.3,

(iii) any and all non-patented or non-patent pending technical information, formulations, compounds, compositions, products, processes, know-how, trade secrets, data, specifications, methods of manufacture or use including but not limited to diagnostic methods and methods for prevention as well as treatment, analytical or characterization methods, characterization results, and other proprietary information, that are:

a. controlled by VCU, and
b. related to the VCU Invention Disclosures listed in Appendix A, and
c. developed, generated, made, conceived or reduced to practice by or on behalf of INVENTOR(S), alone or with others, during the course of research conducted by them, in accordance with Section 2.3.

For purposes hereof, “controlled” means with respect to any technical information, formulations, compounds, compositions, products, processes, know-how, trade secrets, data, specifications, methods of manufacture or use including but not limited to diagnostic methods and methods for prevention as well as treatment, analytical or characterization methods, characterization results, and/or other proprietary information, the right to grant a license or sublicense without violating the terms of any agreement with, without violating any legal rights of, or without requiring the consent of, any third party. For clarity, “controlled” includes the right of LICENSOR to grant a license or sublicense, pursuant to the IIA, to any or all of the foregoing, without violating the terms of any agreement with, without violating any legal rights of, or without requiring the consent of, any third party,
and

(iv) Other technologies, inventions and know-how associated with the VCU Invention Disclosures listed in Appendix A that were discovered or invented by or on behalf of INVENTOR(S) as of the EFFECTIVE DATE, including the following: (a) oxysterols and any steroids or steroid metabolites and any derivatives or analogs thereof (hereinafter "Small Molecules"); (b) enzymes (including amino acid sequences and nucleotide sequences) that make or modify any Small Molecules (hereinafter "Enzymes"); (c) genes that make or express any Small Molecules, or that are affected or modulated by any Small Molecules ("Genes"); (d) molecules such as binding proteins that modulate or otherwise affect any Small Molecules, or that are modulated by or otherwise affected by any Small Molecules ("Modulating Molecules"); (e) compositions of Small Molecules, Enzymes, Genes or Modulating Molecules; (f) methods of making Small Molecules, Enzymes, Genes or Modulating Molecules; and/or (g) uses of Small Molecules, Enzymes, Genes or Modulating Molecules.

1.19 "MAJOR MARKET" means the United States of America or a member country of the European Union.

1.20 "NET SALES" shall mean the amounts received by LICENSEE and its AFFILIATES and SUBLICENSEES from the commercial use of LICENSED PRODUCTS, or the commercial sale of LICENSED PRODUCTS, from non-AFFILIATED third parties in arm's length transactions, less, to the extent such deductions or allowances can be documented by LICENSEE: (i) shipping costs (including freight, postage, handling and standard transportation charges such as insurance and packing and distribution charges), (ii) allowances or credits because of returned, rejected or recalled LICENSED PRODUCTS as actually allowed, (iii) other discounts, credits and allowances including normal and customary quantity discounts, cash discounts (including discounts for prompt payment), and customary trade promotional allowances and credits (including adjustments such as those granted on account of co-pay reduction programs, price adjustments, billing errors, damaged goods, rebates, chargeback rebates, fees, reimbursements or similar payments granted or given to wholesalers or other distributors, buying groups, healthcare insurance carriers, group purchasing organizations, managed health care organizations, wholesalers, pharmacy benefit management or similar organizations, federal, state/provincial, local and other governments, including their agencies, trade customers or other institutions), and discounts mandated by or granted in response to laws or regulations, retroactive price reductions or rebates paid or credited to any governmental authority or agency or third party payor, administrator or contractee, including in respect of any government subsidized program (including without limitation Medicare and Medicaid rebates), and (iv) taxes including import, export, use, excise and sales taxes, tariffs and duties (including customs duties) and other governmental charges imposed on the importation, use or sale of LICENSED PRODUCTS (including without limitation, value-added and withholding taxes). If LICENSED PRODUCTS are sold through intermediaries such as agents, consignees or co-promoters who do not purchase and take title to LICENSED PRODUCTS, royalties shall be due only on sales to those non-AFFILIATED third parties who actually purchase and take title to LICENSED PRODUCTS through such intermediaries. For non-cash and partial-cash sales, NET SALES shall include the fair market value of non-cash consideration received for such sale of the same quantity of LICENSED PRODUCTS. For sales not at arms-length, NET SALES shall be equal to the fair market price of such LICENSED PRODUCTS as when transferred in comparable arms-length transactions. In the event that LICENSED PRODUCTS are used by LICENSEE rather than sold, the parties shall agree upon an appropriate NET SALES price for each such use on which to base a royalty calculation. NET SALES shall not include any amounts received by LICENSEE and/or its AFFILIATES or SUBLICENSEES from the commercial use of LICENSED PRODUCTS, or the commercial sale of LICENSED PRODUCTS, from non-AFFILIATED third parties in arm's length transactions, in any countries where there are no VALID CLAIMS of LICENSED PATENT RIGHTS covering the manufacture, use or sale of LICENSED PRODUCTS in such countries, and there are no VALID CLAIMS of LICENSED PATENT RIGHTS

covering the manufacture of such LICENSED PRODUCTS in the country of manufacture. Royalties shall not be due and payable on any LICENSED PRODUCTS that are provided at no cost as samples, used in the conduct of any non-clinical or pre-clinical studies or clinical trials, testing, promotion or market research, or made available for charitable purposes or for compassionate use.

1.21"NON-INVENTOR(S)" means any VCU/ VA Personnel who is not an INVENTOR.

1.22"NON-INVENTOR IMPROVEMENT(S)" means IMPROVEMENT(S) not falling under the SRA TECHNOLOGY, that are developed, generated, made, conceived or reduced to practice solely by or on behalf of a NON-INVENTOR(S).

1.23"Patent Prosecution Costs" shall have the meaning ascribed to such term in Section 4.5.

1.24"Proprietary Information" means a party's written information, materials and data marked proprietary or confidential or non-written information, materials and data disclosed in whatever form which is identified at the time of disclosure as proprietary or confidential and is reduced to writing and transmitted to the other party and marked proprietary or confidential within sixty (60) days of such non-written disclosure. Proprietary Information shall also have the meaning ascribed to such term in Section 9.19.

1.25"Royalty Holiday" shall have the meaning ascribed to such term in Section 3.5.

1.26"SRA" means the Sponsored Research Agreement by and between VCU and LICENSEE, effective May 7, 2012.

1.27"SRA TECHNOLOGY" means PROJECT TECHNOLOGY (defined in the SRA) and any technology, data, ideas, inventions, discoveries and IMPROVEMENTS, and the intellectual property rights therein and thereto including PROJECT PATENT RIGHTS (defined in the SRA) and enforcement rights, that are developed, generated, made, conceived or reduced to practice, in whole or in part, by INVENTOR(S), alone or with others, directly or indirectly in the performance or as a result of the SRA Project (defined in the SRA).

1.28"SUBLICENSEE" shall mean any non-affiliated third party to whom LICENSEE has granted a SUBLICENSE. SUBLICENSEE shall also mean any non-affiliated third party to whom a SUBLICENSEE has granted a SUBLICENSE. "SUBLICENSE" shall mean an agreement in which LICENSEE or SUBLICENSEE (i) grants any of the rights licensed to LICENSEE hereunder, or (ii) agrees not to assert such rights or to sue, prevent or seek a legal remedy for the practice of any of the rights licensed to LICENSEE hereunder. Notwithstanding the foregoing, a SUBLICENSEE shall not mean a successor entity or an entity that acquires all or substantially all of the stock, business or assets of LICENSEE, or all or substantially all of the stock, business or assets of LICENSEE that relate to the LICENSED TECHNOLOGY or LICENSED PATENT RIGHTS, whether by acquisition, merger, sale of stock, sale of assets or otherwise.

1.29 "SUBLICENSING REVENUE" shall mean payments or fair market value of non-cash consideration received by LICENSEE from a SUBLICENSEE under and in consideration for its SUBLICENSE, including if applicable, license issue fees and other licensing fees, milestone payments or other payments. For any refundable payments made to LICENSEE by a SUBLICENSEE that are subsequently refunded to such SUBLICENSEE, LICENSEE can deduct such amounts from future royalty payments, Annual Minimum Payments and/or milestone payments owed to LICENSOR. In the case where LICENSEE receives a milestone payment from a SUBLICENSEE for the same event that triggers one of the milestone payments owed by LICENSEE to LICENSOR as provided for in Appendix B

subsection 5 (*e.g.*, upon the first filing of an IND with FDA or foreign equivalent in a MAJOR MARKET country), SUBLICENSING REVENUE shall only include the portion of the milestone payment received by LICENSEE from the SUBLICENSEE that is over and above the amount already owed to LICENSOR as provided for in Appendix B, subsection 5. To determine the basis on which SUBLICENSING REVENUE is to be calculated, the following amounts shall be excluded, even if they are paid by a SUBLICENSEE to LICENSEE, including as part of any upfront or milestone payment, whether in cash or as non-cash consideration: royalties; payments to fund ongoing and future research and/or development activities including without limitation in connection with the design and conduct of human clinical trials; payments for the manufacture and supply of LICENSED PRODUCT or excipients or components thereof for pre-clinical, clinical or commercial use; equity investments in LICENSEE (including without limitation the sale of capital stock of LICENSEE or other securities convertible into capital stock of LICENSEE), provided, however, that if in consideration for its sublicensing rights, a SUBLICENSEE makes an equity investment in LICENSEE and pays a premium on equity, then SUBLICENSING REVENUE shall include that portion which is a premium of fifteen percent (15%) or more on equity; or any amounts pursuant to a sale of all or substantially all of the business or assets of LICENSEE related to the LICENSED TECHNOLOGY or LICENSED PATENT RIGHTS (whether by acquisition, merger, sale of stock, sale of assets or otherwise). For clarity, SUBLICENSING REVENUE shall not include payments or fair market value of non-cash consideration received by a SUBLICENSEE from a third party (including a sub-SUBLICENSEE) under and in consideration for a sub-SUBLICENSE. However, SUBLICENSING REVENUE shall include any proceeds received by a SUBLICENSEE from a third party (including a sub-SUBLICENSEE) under and in consideration for a sub-SUBLICENSE that are subsequently paid to LICENSEE in consideration for a sub-SUBLICENSE.

1.30 "VALID CLAIM" shall mean a claim of an issued and unexpired patent within the LICENSED PATENT RIGHTS that has not been (i) cancelled with prejudice, (ii) declared invalid or unenforceable by decision of a court of competent jurisdiction or other governmental authority, (iii) admitted to be invalid or unenforceable through reissue, disclaimer, or otherwise, or (iv) abandoned.

II. GRANT

2.1 LICENSOR hereby grants to LICENSEE an exclusive, royalty bearing, worldwide license under LICENSED TECHNOLOGY and LICENSED PATENT RIGHTS to develop, make, have made, use, offer to sell, sell, export and import LICENSED PRODUCTS and to use, practice and otherwise exploit methods embodying LICENSED TECHNOLOGY and/or that are disclosed in, covered or claimed by LICENSED PATENT RIGHTS, with the right to SUBLICENSE others through multiple tiers of sublicensees under the terms of Article VIII, throughout the term hereof in the FIELD OF USE. This grant shall be subject to the payment by LICENSEE to LICENSOR of all consideration as provided in this Agreement, and shall be further subject to the rights retained by LICENSOR, VCU, and VA:

(a) subject to Section 9.20, publish the scientific findings from research related to LICENSED PATENT RIGHTS,

(b) to practice under the LICENSED PATENT RIGHTS for internal educational, research, and other internal non-commercial purposes, except that such purposes shall not include any testing or other use in humans without the LICENSEE's prior written consent which may be withheld in its sole discretion. LICENSOR will not file for any regulatory approvals to test or market any LICENSED PRODUCTS anywhere in the world,

(c) Subject to the limitations set forth in Section 2.1(b) above, such reservation shall include the right to extend such right to practice under the LICENSED PATENT RIGHTS for internal educational and research purposes (but not for patient care and treatment, or any other internal purpose) to subsequent employers of any of the INVENTORS, but only to the extent that such employers are not-for-profit organizations, and

(d) For biological materials and/or research tools that are covered under the LICENSED TECHNOLOGY and could be considered a NIH-funded research resource (collectively and hereinafter "Materials"), such reservation shall further include the right to provide such Materials and to grant licenses under the LICENSED PATENT RIGHTS, to not-for-profit and governmental institutions for their non-commercial, internal research and scholarly use only, in accordance with the NIH Guidelines for Obtaining and Disseminating Biomedical Research Resources (as published in the U.S. Federal Register / vol. 64, No. 246 - 12/23/99). Notwithstanding the foregoing, the parties understand and agree that the compounds, compositions, formulations and products that are claimed or covered in any of the LICENSED PATENT RIGHTS and/or VCU Invention Disclosures listed in Appendix A, in each case during the term of this Agreement, including any Small Molecules, Enzymes, Genes or Modulating Molecules, and any related know how, and/or processes and methods (which processes or methods are necessary or useful to develop, manufacture, use, offer for sale, sell, import or export such compounds, compositions, formulations or products), are not and shall not be deemed Materials under this Section 2.1(d).

(e) LICENSOR agrees to notify LICENSEE in writing no less than thirty (30) days prior to taking any of the actions described in Sections 2.1(c) or 2.1(d) above.

(f) Under the IIA, VA is obligated to receive and treat as confidential, LICENSEE's Proprietary Information that LICENSOR provides to the VA in fulfillment of its obligations under the IIA and not disclose such Proprietary Information without the prior written consent of LICENSOR. LICENSOR shall promptly notify LICENSEE in writing if during the term hereof, the IIA is amended, expires or terminates, or if the confidentiality obligations of VA under the IIA change.

2.2Notwithstanding anything herein to the contrary, any and all licenses and other rights granted hereunder are limited by and subject to the rights and requirements of the United States Government which may attach as a result of Government sponsorship of research at VCU, in which the invention covered by the LICENSED PATENT RIGHTS was conceived or reduced to practice, as set forth in 35 U.S.C. §§200-206, 37 C.F.R. Part 401 and in the relevant Government research contracts with VCU, and as such rights and requirements may be amended or modified by law. To the extent applicable, such rights and requirements include without limitation (i) the grant of a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the Government any of the LICENSED PATENT RIGHTS throughout the world (as set forth in 35 U.S.C. §202(c)(4)), and (ii) the requirement that LICENSED PRODUCTS used or sold in the United States will be manufactured substantially in the United States (as set forth in 35 U.S.C. §204).

2.3LICENSOR shall promptly disclose to LICENSEE in writing, all SRA TECHNOLOGY, INVENTOR IMPROVEMENTS, COLLABORATION IMPROVEMENTS, and NON-INVENTOR IMPROVEMENTS. Such SRA TECHNOLOGY, INVENTOR IMPROVEMENTS, COLLABORATION IMPROVEMENTS, and NON-INVENTOR IMPROVEMENT(S) shall be added to the LICENSED TECHNOLOGY subject to the following conditions and in the following manner:

a. Without additional consideration, all SRA TECHNOLOGY is hereby included in LICENSED TECHNOLOGY and thereby made subject to the exclusive license granted by LICENSOR to LICENSEE hereunder. Appendix A shall be updated periodically to reflect the addition of such SRA TECHNOLOGY.

b. For a period of five (5) years from the EFFECTIVE DATE of this Agreement and without additional consideration, all INVENTOR IMPROVEMENT(S) are hereby included in LICENSED TECHNOLOGY and thereby made subject to the exclusive licenses granted by LICENSOR to LICENSEE hereunder, except for those INVENTOR IMPROVEMENTS that are subject to pre-existing third party obligations under sponsored research agreements. LICENSOR shall promptly and in sufficient detail notify LICENSEE in writing of any such pre-existing third party obligations. LICENSOR will use its best efforts to work with VCU to ensure that any third party obligations under sponsored research agreements are unrelated to LICENSED TECHNOLOGY. Appendix A shall be updated periodically to reflect the addition of such INVENTOR IMPROVEMENT(S).

c. For a period of five (5) years from the EFFECTIVE DATE of this Agreement and without additional consideration, all COLLABORATION IMPROVEMENTS are hereby included in LICENSED TECHNOLOGY and thereby made subject to the exclusive licenses granted by LICENSOR to LICENSEE hereunder, provided all NON-INVENTORS agree in writing to inclusion of their interest in such COLLABORATION IMPROVEMENTS in the LICENSED TECHNOLOGY, except for those COLLABORATION IMPROVEMENTS that are subject to pre-existing third party obligations under sponsored research agreements. LICENSOR will use its best efforts to work with VCU to ensure that any third party obligations under sponsored research agreements are unrelated to LICENSED TECHNOLOGY. LICENSOR shall endeavor in good faith to have all NON-INVENTORS agree in writing to inclusion of their interest in COLLABORATION IMPROVEMENT(S) in the LICENSED TECHNOLOGY. If a NON-INVENTOR does not agree in writing to inclusion of his/her interest in such COLLABORATION IMPROVEMENT in the LICENSED TECHNOLOGY, then the NON-INVENTOR's interest in such COLLABORATION IMPROVEMENT will not be included in LICENSED TECHNOLOGY and LICENSEE will have no rights to said NON-INVENTOR's interest in such COLLABORATION IMPROVEMENT. For clarity, even if a NON-INVENTOR does not agree in writing to inclusion of his/her interest in such COLLABORATION IMPROVEMENT in the LICENSED TECHNOLOGY, LICENSEE shall nevertheless have a non-exclusive license to the COLLABORATION IMPROVEMENT. For purposes of this Section 2.3 (including this Section 2.3(c), Section 2.3 (b) above and 2.3(d) below), "pre-existing" means existing prior to the date on which an INVENTOR IMPROVEMENT, NON-INVENTOR IMPROVEMENT or COLLABORATION IMPROVEMENT (as the case may be) is made. LICENSOR shall promptly and in sufficient detail notify LICENSEE in writing of any such pre-existing third party obligations. If there are not any such pre-existing third party obligations and all NON-INVENTORS agree in writing to inclusion of their interest in such COLLABORATION IMPROVEMENTS, then such COLLABORATION IMPROVEMENTS are hereby included in LICENSED TECHNOLOGY, made subject to the exclusive licenses granted by LICENSOR to LICENSEE hereunder and added to Appendix A upon their conception. Appendix A shall be updated periodically to reflect the addition of such COLLABORATION IMPROVEMENT(S).

d. For a period of five (5) years from the EFFECTIVE DATE of this Agreement, LICENSOR hereby grants to LICENSEE an exclusive option to include any NON-INVENTOR

IMPROVEMENT in the LICENSED TECHNOLOGY, which option may be exercised by LICENSEE, provided:

(i) there are no pre-existing third party obligations that would conflict with this Agreement. LICENSOR shall promptly and in sufficient detail notify LICENSEE in writing of any such pre-existing third party obligations that would conflict with this Agreement.

(ii) All NON-INVENTORS must agree in writing to inclusion of their NON-INVENTOR IMPROVEMENT in the LICENSED TECHNOLOGY. LICENSOR shall endeavor in good faith to have all NON-INVENTORS agree in writing to inclusion of their NON-INVENTOR IMPROVEMENT(S) in the LICENSED TECHNOLOGY. If a NON-INVENTOR does not agree in writing to inclusion of such NON-INVENTOR IMPROVEMENT in the LICENSED TECHNOLOGY, then the NON-INVENTOR IMPROVEMENT will not be included in the LICENSED TECHNOLOGY and LICENSEE will have no rights to said NON-INVENTOR IMPROVEMENT.

(iii) For each NON-INVENTOR IMPROVEMENT that LICENSEE, at its written election, wishes to be included in LICENSED TECHNOLOGY, LICENSEE pays LICENSOR a twenty-five thousand dollar ($25,000) improvement fee.

(iv) If all of the above conditions are met, such NON-INVENTOR IMPROVEMENT shall be included in the LICENSED TECHNOLOGY, added to Appendix A and made subject to the exclusive licenses granted by LICENSOR to LICENSEE hereunder. Appendix A shall be updated periodically to reflect the addition of such NON-INVENTOR IMPROVEMENT(S).

e. LICENSOR will keep LICENSEE apprised of its efforts to obtain the written agreement of NON-INVENTOR(S) as provided for in Sections 2.3(c) and (d), and will notify LICENSEE promptly in writing if a NON-INVENTOR refuses to include his or her interest in a COLLABORATION IMPROVEMENT or NON-INVENTOR IMPROVEMENT in the LICENSED TECHNOLOGY. Unless and until a NON-INVENTOR refuses to agree to include his or her interest in a COLLABORATION IMPROVEMENT or a NON-INVENTOR IMPROVEMENT in the LICENSED TECHNOLOGY, no rights or licenses to any COLLABORATION IMPROVEMENT or NON-INVENTOR IMPROVEMENT will be discussed, negotiated, offered or granted by LICENSOR to any third party, nor will any COLLABORATION IMPROVEMENTS or NON-INVENTOR IMPROVEMENTS be transferred by LICENSOR or assigned by LICENSOR to a third party.

III. PAYMENT PROVISIONS

3.1 In consideration for the rights, privileges and licenses granted under this Agreement, the LICENSEE shall pay to LICENSOR the fees and royalties specified in Article IV and Appendix B, attached hereto and incorporated herein by reference.

3.2 With each report submitted under Section 5.2 of this Agreement, LICENSEE shall make all payments to LICENSOR that are due and payable under Article III of this Agreement. If no royalties are due, LICENSEE shall so report.

3.3 LICENSEE shall be obligated to pay royalties on all NET SALES of LICENSED PRODUCTS that are sold commercially under this license as described in Appendix B, regardless of whether such

NET SALES of LICENSED PRODUCTS occurred prior to the EFFECTIVE DATE of this Agreement or after the termination of this Agreement but only if pursuant to Section 7.5. LICENSEE shall continue to make reports concerning royalties on NET SALES of LICENSED PRODUCTS payable in accordance with Article III after termination of the license, until such time as all such LICENSED PRODUCTS produced under the license and sold pursuant to Section 7.5, have been sold or destroyed. Concurrent with the submittal of each post-termination report, LICENSEE shall pay LICENSOR all applicable royalties.

3.4 All payments due the LICENSOR must be paid in U.S. currency to the LICENSOR. The LICENSEE must convert NET SALES invoiced in foreign currency into equivalent U.S. currency at the exchange rate for the foreign currency prevailing as of the last day of the reporting period, as reported in the *Wall Street Journal*®. Royalty payments shall be based on NET SALES of LICENSED PRODUCT in any country where a VALID CLAIM of a LICENSED PATENT RIGHT covering a LICENSED PRODUCT or its manufacture, use or sale is in effect, and on NET SALES of LICENSED PRODUCT in a country to which the LICENSED PRODUCT has been exported, but no VALID CLAIM of a LICENSED PATENT RIGHT covers the LICENSED PRODUCT or its manufacture, use or sale in such country of sale, but the LICENSED PRODUCT was produced in a country where a VALID CLAIM of a LICENSED PATENT RIGHT covering the manufacture of such LICENSED PRODUCT was in effect at the time of such manufacture. LICENSEE agrees to pay interest of 1.5% per month, the interest being compounded monthly, or the maximum rate allowed by law, whichever is less, on any delinquent undisputed payments to LICENSOR. LICENSEE shall calculate the correct late payment charge, and shall add it to each such late payment.

3.5 Royalty Holiday. LICENSEE shall not be obligated to pay royalties to LICENSOR hereunder with respect to a LICENSED PRODUCT while there is a pending third party claim of actual or alleged infringement or misappropriation of intellectual property rights as a result of the composition of matter, manufacture, use, sale, offer for sale or import of such LICENSED PRODUCT (such period of time to be referred to as a "Royalty Holiday"). After such third party claim has been finally resolved (either through a final and binding settlement or by a determination by a court of competent jurisdiction from which an appeal cannot be taken), LICENSEE's royalty payment obligation shall recommence and any royalty payments that accrued but were not paid to LICENSOR during such Royalty Holiday shall be paid to LICENSOR subject to and in accordance with Appendix B, subsection 2(d). For the purposes of clarity, such Royalty Holiday is only applicable when the alleged infringement pertains to the LICENSED TECHNOLOGY licensed to LICENSEE under this Agreement and does not apply when aspects of the LICENSED PRODUCT not relating to the LICENSED TECHNOLOGY are alleged to infringe.

IV. DILIGENCE AND PATENT PROSECUTION

4.1 The LICENSEE will use its COMMERCIALLY REASONABLE EFFORTS to bring one or more LICENSED PRODUCTS to market and to market LICENSED PRODUCTS throughout the life of this Agreement. It is agreed that LICENSEE may meet its obligations under Sections 4.1 and 4.2 of this Article IV through one or more AFFILIATES, SUBLICENSEES, co-promoters, sales representatives, distributors and/or subcontractors. Moreover, LICENSEE shall not be required to obtain regulatory approval for, or market and sell, LICENSED PRODUCTS in countries other than those where, in LICENSEE's reasonable opinion, there is a significant market for LICENSED PRODUCTS.

4.2 To be in compliance with Section 4.1, the LICENSEE must meet the following diligence requirements:

(i) LICENSEE shall continue to invest at least one hundred thousand dollars ($100,000)

each calendar year, including under the SRA, for development of one or more LICENSED PRODUCTS until the first LICENSED PRODUCT is sold.

(ii) LICENSEE shall use its COMMERCIALLY REASONABLE EFFORTS to develop and file for regulatory approval of one or more LICENSED PRODUCTS in a timely and diligent manner.

(iii) In the event that LICENSEE ceases to progress development of all LICENSED PRODUCTS prior to the first filing of a New Drug Application (NDA) or foreign equivalent for the first LICENSED PRODUCT, or ceases to market all LICENSED PRODUCTS in a MAJOR MARKET after having launched a LICENSED PRODUCT in such MAJOR MARKET (unless such approval has been revoked), then LICENSEE shall immediately notify LICENSOR of its decision to either cease to develop or cease to market, as applicable. Thereafter, the parties shall meet and discuss, in good faith, LICENSEE's reasons for such cessation and a possible continued path forward. If such cessation of COMMERCIALLY REASONABLE EFFORTS to develop or commercialize is due to safety, efficacy, legal or regulatory impediment or other events beyond the reasonable control of LICENSEE, its AFFILIATES and/or SUBLICENSEES, then LICENSEE shall have no obligation beyond the above notification requirement. Otherwise, LICENSEE shall, within ninety (90) days of such notification, propose a commercially reasonable plan to address, in a timely manner, the problem causing the cessation of using its COMMERCIALLY REASONABLE EFFORTS to develop or commercialize and shall have an additional sixty (60) days to resume or commence COMMERCIALLY REASONABLE EFFORTS with respect to the same or a different LICENSED PRODUCT. In the event that LICENSEE does not resume or commence COMMERCIALLY REASONABLE EFFORTS within the one-hundred and fifty (150) day period, LICENSOR shall have the option to terminate this Agreement upon sixty (60) days written notice to LICENSEE unless LICENSEE resumes or commences using its COMMERCIALLY REASONABLE EFFORTS to develop or market at least one LICENSED PRODUCT during such sixty (60) day notice period.

4.3 Article IV is a material term of this Agreement, without which the license granted under Article II would not have been made, and the LICENSEE's failure to perform in accordance with Sections 4.1 and 4.2 would constitute a material breach of this Agreement.

4.4 LICENSOR shall have exclusive responsibility for the preparation, filing, prosecution, and maintenance of the LICENSED PATENT RIGHTS, including choice of patent counsel; provided, however, that if LICENSOR decides to have the filing, prosecution and/or maintenance of any LICENSED PATENT RIGHTS handled by an outside law firm, whether foreign or domestic, LICENSOR will not select any law firm or lawyer that is not reasonably acceptable to LICENSEE. LICENSOR shall keep LICENSEE fully informed of the preparation and filing of patent applications and of patent prosecution and the maintenance of patents in relation to the LICENSED PATENT RIGHTS, and LICENSEE shall be given an opportunity to review and provide input with respect thereto, including the right to comment on strategy and prosecution and make suggestions for claims, and LICENSOR agrees to take into account LICENSEE's input. Without limiting the foregoing, LICENSOR shall send to LICENSEE and LICENSEE shall receive drafts of proposed patent applications, patent office responses and foreign counsel instructions at least thirty (30) days, where practical, before their submission. LICENSOR shall provide LICENSEE with all reasonable opportunities, including direct access to LICENSOR's patent counsel, to participate in the drafting of applications, petitions, responses to office actions and other inquiries of patent examining authorities, and in the conduct of interviews with, and other oral arguments to, such authorities. LICENSEE shall also have the right to make requests to LICENSOR as to when and where to file patent applications, continuations, divisionals, continuations-in-part, substitutes, renewals, reissues, extensions, confirmations, reexaminations and registrations with

respect to the LICENSED PATENT RIGHTS and LICENSOR will use reasonable efforts to accommodate LICENSEE's requests.

4.5 LICENSEE shall reimburse all reasonable documented outside legal expenses, not already reimbursed by LICENSEE, incurred by LICENSOR after the Effective Date of the Option Agreement and not already reimbursed by LICENSEE as of the EFFECTIVE DATE, and during the term of this Agreement by LICENSOR in filing, prosecuting and maintaining the LICENSED PATENT RIGHTS (the "Patent Prosecution Costs"), within thirty (30) days after receipt of an undisputed invoice from LICENSOR. Any payments to LICENSOR's counsel are made with the understanding that such payments do not create an attorney-client relationship between LICENSEE and such counsel.

4.6 LICENSOR or its patent counsel shall inform LICENSEE in a timely manner (in writing, including via email) as to all developments with respect to the LICENSED PATENT RIGHTS on a worldwide basis, including all actions necessary for the filing, prosecution, issuance and maintenance of LICENSED PATENT RIGHTS (including promptly furnishing LICENSEE with copies of all correspondence in relation thereto including copies of communications from the Patent and Trademark Office, including foreign patent offices, and correspondence from foreign patent counsel) and shall promptly furnish to LICENSEE copies of all papers received and filed in connection with the prosecution thereof in sufficient time for LICENSEE to comment thereon. LICENSEE shall promptly instruct LICENSOR in writing whether to take such action at LICENSEE's expense. Provided LICENSOR has timely notified LICENSEE of any proposed actions as provided for herein, if LICENSOR does not receive from LICENSEE written or oral instruction to take the action at issue within fifteen (15) days prior to the statutory bar date for such action, LICENSOR shall have no obligation to take or have taken such action to protect the LICENSED PATENT RIGHTS at issue, even if the result is the irrevocable loss of rights.

4.7If LICENSOR decides to file patent applications, continuations, divisionals, continuations-in-part, substitutes, renewals, reissues, extensions, confirmations, reexaminations or registrations with respect to the LICENSED PATENT RIGHTS in any countries other than those countries where LICENSEE has directed LICENSOR to file under Section 4.4, LICENSOR shall be responsible for all of the costs, expenses and fees associated with the LICENSED PATENT RIGHTS in such countries. If LICENSEE declines to pay in full any reasonable, documented outside legal expenses necessary for the filing, protection or maintenance of any LICENSED PATENT RIGHTS that LICENSEE directed LICENSOR to file under Section 4.4, LICENSOR shall have the right to (i) abandon the LICENSED PATENT RIGHTS for which payment has not been made in full, at LICENSOR's sole discretion, or (ii) incur those costs at its own expense. In the former case, the royalty rate for NET SALES of LICENSED PRODUCTS sold in the country where all such LICENSED PATENT RIGHTS have been abandoned and there are no VALID CLAIMS of any LICENSED PATENT RIGHTS in such country covering the manufacture, use or sale of LICENSED PRODUCT in such country, will be reduced by fifty percent (50%). In the latter case in which LICENSOR continues to pursue patent protection at its own expense, LICENSOR may require LICENSEE to pay royalties for NET SALES of LICENSED PRODUCTS in that country as specified in Appendix B.

4.8 If LICENSOR decides to abandon prosecution or maintenance of any patent application or patent within the LICENSED PATENT RIGHTS in a country where LICENSEE has requested LICENSOR to make and maintain such filing or patent, LICENSOR shall provide LICENSEE written notice of LICENSOR's intent to abandon such application or patent in sufficient time to permit LICENSEE in its discretion to continue such prosecution or maintenance. In such event, LICENSEE shall have the right to continue prosecution of said application, or maintenance of such patent, at its own expense, on behalf of LICENSOR and LICENSEE. In such event, LICENSOR shall execute all documents and perform such acts as may be reasonably necessary for LICENSEE to continue such prosecution or maintenance.

LICENSOR shall also notify LICENSEE in writing if LICENSOR decides not to file any patent applications, continuations, divisionals, continuations-in-part, substitutes, renewals, reissues, extensions, confirmations, reexaminations or registrations with respect to any of the LICENSED PATENT RIGHTS which may be suggested by LICENSEE. Such notice shall be given in sufficient time to permit LICENSEE in its discretion to prepare such filings, in which case LICENSOR shall execute all documents and perform such acts as may be reasonably necessary for LICENSEE to make such filings.

4.9 LICENSEE shall reimburse Patent Prosecution Costs as follows: LICENSEE shall have the opportunity to review and comment on the bills of any outside law firm before LICENSOR pays such bills. LICENSOR shall submit detailed invoices to LICENSEE for all reasonable and necessary Patent Prosecution Costs paid by LICENSOR in monitoring, drafting, filing, prosecuting and maintaining LICENSED PATENT RIGHTS, including outside counsel fees, patent office fees for filing, prosecution, reissue, reexamination and issue, maintenance fees, fees for foreign filings and PCT filings. No part of any of LICENSOR's employees' salaries shall be reimbursed hereunder. Moreover, LICENSEE shall not reimburse LICENSOR for any Patent Prosecution Costs incurred for new foreign filings or new PCT filings that are undertaken after the EFFECTIVE DATE without LICENSEE's prior written authorization which may be via email.

4.10 LICENSOR shall have the right to immediately terminate this Agreement in the event that LICENSEE knowingly challenges, directly or indirectly or at written urging of a third party on behalf of LICENSEE, whether as a claim, a cross-claim, counterclaim, or defense, the validity or enforceability of any of the LICENSED PATENT RIGHTS before any court, arbitrator, or other tribunal or administrative agency in any jurisdiction, and LICENSEE does not cease (or cause to cease) such challenge within thirty (30) days after receiving written notice thereof from LICENSOR.

V. REPORTING OBLIGATIONS

5.1 Progress Report. On or before April 1 and October 1 of each year until the first commercial sale of the first LICENSED PRODUCT, LICENSEE shall make a written semi-annual report to LICENSOR covering the preceding six (6) months regarding the progress of LICENSEE, its AFFILIATES and/or SUBLICENSEES toward commercialization of LICENSED PRODUCTS, including those COMMERCIALLY REASONABLE EFFORTS that have been used by LICENSEE, its AFFILIATES and/or SUBLICENSEES to develop and file for regulatory approval of one or more LICENSED PRODUCTS. Such report shall include, as a minimum, information sufficient to enable LICENSOR to satisfy reporting requirements of the U.S. Government (provided LICENSEE is given written notice of the required information and sufficient time to furnish such information in order for LICENSOR to meet such U.S. Government requirements), and for LICENSOR to ascertain progress by LICENSEE toward meeting the diligence requirements of Sections 4.1 and 4.2. After the first commercial sale of the first LICENSED PRODUCT, LICENSEE's reporting obligations to LICENSOR shall be as set forth in Section 5.2.

5.2 LICENSEE, within sixty (60) days after each CALENDAR QUARTER of each year following the first commercial sale of a LICENSED PRODUCT, shall deliver to LICENSOR true and accurate reports, pertaining to NET SALES of LICENSED PRODUCTS as follows:

a) the identity of each LICENSED PRODUCT being developed, marketed and/or sold;
b) the number of each LICENSED PRODUCT sold in each country;
c) NET SALES of LICENSED PRODUCTS sold by LICENSEE, its AFFILIATES and all SUBLICENSEES, prepared in accordance with United States generally accepted accounting principles, on a country by country basis, for each LICENSED PRODUCT;
d) any and all allowable deductions made by LICENSEE to calculate NET SALES;

e) names and addresses of all SUBLICENSEES of LICENSEE; and
f) total royalties due.

5.3 LICENSEE shall keep full, true and accurate books of account for the purpose of showing the amounts payable to LICENSOR hereunder. Said books of account shall be kept at LICENSEE's principal place of business. No more frequently than once per year, LICENSOR, at its expense, may within forty-five (45) days of its written request, have reviewed such books of account at LICENSEE's principal place of business, to verify the accuracy of LICENSEE'S payments made hereunder. Such review shall be performed by an independent third party certified public accounting firm designated by LICENSOR and reasonably acceptable to LICENSEE, during regular business hours and under conditions of confidentiality. Under no circumstances shall LICENSOR or the independent third party certified public accounting firm have access to any of the books and records of any SUBLICENSEE. LICENSOR may, however, require that LICENSEE perform or have performed, no more than once per year, a review of a SUBLICENSEE's books of account to verify the accuracy of payments made by a SUBLICENSEE to LICENSEE under any SUBLICENSE, the costs and expenses of which shall be reimbursed by LICENSOR. Such verification by LICENSOR hereunder may be conducted for three (3) years following the end of the calendar year to which the verification pertains. Should such inspection, however, lead to the discovery of a greater than five percent (5%) discrepancy in reporting to LICENSOR's detriment, LICENSEE shall pay the full reasonable, documented costs of such inspection. LICENSEE shall pay any amounts such inspection reveals to be due and owing within thirty (30) days of the receipt of an invoice for same. If such inspection reveals any overpaid amounts, LICENSEE can deduct such amounts from future royalty payments owed to LICENSOR.

VI. INFRINGEMENT

6.1LICENSEE acknowledges and agrees that other than as expressly provided for in this Agreement, all rights licensed by the LICENSOR hereunder are licensed "as is" and without any representation, indemnification or warranty with respect to possible infringement of third party rights. LICENSOR and LICENSEE shall promptly notify the other party in writing with respect to any claim, suit or other action brought by a third party alleging that the composition of matter, manufacture, use, import, offer for sale or sale of a LICENSED PRODUCT infringes or misappropriates any third party intellectual property rights. In the event of a third party infringement action against either party with respect to any LICENSED PRODUCTS that are developed, manufactured, marketed or sold by or on behalf of LICENSEE, LICENSEE will, subject to subsections (i) through (iii) of Section 9.5, defend LICENSOR, VA and VCU at LICENSEE's expense, with the understanding that breaching such obligation may result in a default judgment against LICENSEE, its AFFILIATES, SUBLICENSEES, and/or LICENSOR (however, LICENSEE's failure to defend shall not prevent VCU, VA and LICENSOR from defending themselves). LICENSEE shall indemnify, defend and hold VCU, VA and LICENSOR harmless from any judgment to the extent resulting from the infringement of third party intellectual property rights by LICENSED PRODUCTS that are developed, manufactured, marketed or sold by or on behalf of LICENSEE, and without limitation shall pay any damages awarded in any such judgment against Indemnitee (as defined in Section 9.5), except where such damages are attributable to the negligence, intentional misconduct, violation of law or regulation or breach of this Agreement by any Indemnitee or VCU/VA Personnel. LICENSOR will cooperate as requested by LICENSEE, and will be compensated by LICENSEE for its reasonable documented out-of-pocket expenses incurred in such cooperation, which LICENSOR will only be required to expend if LICENSEE has approved same in writing for reimbursement. No settlement, consent judgment, or other voluntary final disposition of any suit that would affect the validity, scope or enforceability of the LICENSED PATENT RIGHTS, by estoppel, admission or otherwise, or the LICENSOR's rights in or to same, may be entered into without the consent of LICENSOR, not to be unreasonably withheld, delayed or conditioned such as upon additional consideration.

6.2 LICENSEE and LICENSOR shall promptly inform each other in writing of any alleged infringement of the LICENSED PATENT RIGHTS by a third party.

6.3 During the term of this Agreement, LICENSEE will have the primary right, but shall not be obligated, to prosecute at its own expense all enforcement actions against alleged or actual infringements of the LICENSED PATENT RIGHTS and, in furtherance of such right, LICENSEE may include LICENSOR, as a party plaintiff in any such suit, provided that LICENSEE pays the reasonable, documented, out-of-pocket third party costs and expenses of LICENSOR incurred in such joinder and has the right to approve LICENSOR's outside counsel in such joinder, such approval not to be unreasonably withheld. LICENSEE's right also includes without limitation, the right to defend any action for declaratory judgment of non-infringement or invalidity, and instituting, defending and settling all infringement and declaratory judgment actions at its own expense and through counsel of its own choosing. LICENSOR shall provide reasonable assistance to LICENSEE with respect to any such suits. If LICENSOR is not requested by LICENSEE to be included in any such suit, LICENSOR shall have the right to participate with counsel of its own choosing and at its own expense, in any action or suit under this Section 6.3. If LICENSOR makes any statements other than to LICENSEE or LICENSOR's counsel regarding the infringement of LICENSED PATENT RIGHTS, LICENSOR shall be solely responsible for the costs and expenses of any declaratory judgment action relating thereto.

6.4 LICENSEE shall have three (3) months after having been notified of any alleged infringement to investigate whether infringement can be established or if an enforcement action should be taken. If LICENSEE determines that infringement exists, or that any action should be taken, then it shall have an additional three (3) months to negotiate in good faith with the alleged infringer to resolve the dispute or, at LICENSEE's election, to commence prosecuting an infringement action (the filing period). If LICENSEE (a) at any time decides not to pursue an action against the alleged infringer, or (b) fails to commence negotiating or prosecuting an action before the end of the filing period, then LICENSEE shall notify LICENSOR of its intention not to bring suit against any alleged infringer. In those events only, LICENSOR shall have the right, but shall not be obligated, to prosecute at its own expense any infringement of the LICENSED PATENT RIGHTS, and LICENSEE hereby agrees at its discretion and upon terms to be mutually agreed by the parties, to either be named as a plaintiff in any such proceedings or to assign its rights to sue for infringement. LICENSOR shall pay all of LICENSOR's costs and reasonable attorney fees incurred in such action brought by LICENSOR under this Section 6.4. No settlement, consent judgment, or other voluntary final disposition of the suit shall be entered into without the prior written consent of LICENSEE, which consent shall not be unreasonably withheld, and LICENSOR may not settle any such action whereby LICENSOR grants a license to a third party under any LICENSED PATENT RIGHTS without the prior written consent of LICENSEE, which consent may be withheld by LICENSEE in its sole discretion.

6.5 In the event that LICENSOR shall undertake the enforcement and/or defense of the LICENSED PATENT RIGHTS by litigation, any monetary recovery by LICENSOR shall be divided equally between LICENSOR and LICENSEE, after each party recovers its attorneys fees and court costs and other related outside documented costs and expenses. In the event that LICENSEE undertakes the enforcement and/or defense of the LICENSED PATENT RIGHTS by litigation, any monetary recovery by LICENSEE shall be treated as NET SALES hereunder and LICENSEE shall pay the royalties thereon as provided for herein, after each party recovers its attorneys and court costs and other related outside documented costs and expenses.

6.6 Each party will promptly notify the other party in writing if such party institutes any action or suit with regard to third party infringement of the LICENSED PATENT RIGHTS, and will in a timely manner keep the other party informed with regard to such action or suit and any related proceedings. Except as otherwise provided for herein, each party shall bear its own costs and expenses of prosecuting

any enforcement action hereunder. Distribution of any recovered amounts shall be governed by Section 6.5. In any infringement suit that either party may institute to enforce the LICENSED PATENT RIGHTS pursuant to this Agreement, the other party hereto shall, at the request of the party initiating such suit and upon reasonable notice, cooperate in all respects and, to the extent possible, have its employees testify when requested and make available relevant records, papers, information samples, models, specimens and the like.

6.7 LICENSEE shall have the sole right, subject to approval by LICENSOR, which shall not be unreasonably withheld, delayed or conditioned such as upon additional consideration, in accordance with the terms and conditions herein, to grant a SUBLICENSE to any alleged infringer under the LICENSED PATENT RIGHTS. Prior to the payment by LICENSEE to LICENSOR of any SUBLICENSING REVENUE based on amounts received from an alleged infringer as specified in Article III, LICENSOR shall be reimbursed for any and all documented out-of-pocket expenses incurred by it, if any, in connection with any suit or action against the alleged infringer, prior to the grant of the SUBLICENSE to the alleged infringer.

6.8 In the event that any legal action brought by a third party alleging invalidity or noninfringement of any of the LICENSED PATENT RIGHTS is brought against LICENSEE or LICENSOR or VCU, LICENSEE, at its option, shall have the right within thirty (30) days after the commencement of such action, to intervene and take over the sole defense of the action at its own expense. If LICENSEE chooses not to intervene, LICENSOR shall have the option to intervene and take over the sole defense at its own expense.

VII. TERM AND TERMINATION

7.1 This Agreement is in full force and effect from the EFFECTIVE DATE and remains in effect until the expiration of the last to expire LICENSED PATENT RIGHTS, unless sooner terminated by operation of law or by acts of either of the parties in accordance with the terms of this Agreement. On and after the expiration of this Agreement, LICENSEE shall have a fully paid up, royalty-free, irrevocable, perpetual, worldwide, fully sublicensable, non-exclusive right and license to use, practice or have practiced, and otherwise exploit the LICENSED TECHNOLOGY in the FIELD OF USE.

7.2 LICENSEE may terminate this Agreement at any time for any reason or no reason by giving LICENSOR thirty (30) days written notice. In the event of termination of this Agreement by LICENSEE, LICENSEE shall have no further rights under this Agreement; however, LICENSEE will remain obligated for any royalties due or fees accrued or other expenses incurred for which LICENSEE is responsible hereunder, up until the date of termination including royalty on NET SALES of inventory of LICENSED PRODUCTS in stock after the date of termination.

7.3 LICENSOR may terminate this Agreement upon written notice to LICENSEE if LICENSEE commits a material breach or a material default in the performance of LICENSEE's obligations under this Agreement and, within ninety (90) days (thirty (30) days for non-payment of any undisputed material sum) after receipt of written notice of such material breach or material default from LICENSOR (or in the case of a material breach or material default that cannot be cured in ninety (90) days, within a reasonable period under the circumstances so long as LICENSEE is diligently proceeding to cure such material default or material breach), LICENSEE fails to cure such material breach or material default. Examples of such a material breach or material default include:

a. LICENSEE fails to pay on the due date any undisputed material sum due under Article III and Appendix B of this Agreement,

b. LICENSEE fails to provide reports on the due date specified under Article V of this Agreement; and
c. LICENSEE fails to comply with diligence requirements as specified in Sections 4.1 and 4.2 of this Agreement.

7.4The LICENSEE must provide notice to the LICENSOR of its intention to file a voluntary petition in bankruptcy or, where known to the LICENSEE, of another party's intention to file an involuntary petition in bankruptcy for the LICENSEE, said notice must be received by the LICENSOR at least thirty (30) days prior to filing such petition if practicable. LICENSOR may terminate this Agreement upon written notice to LICENSEE following the receipt of such notice at its sole discretion. The LICENSEE's failure to provide such notice to LICENSOR will be deemed a material, pre-petition, incurable breach of this Agreement and the Agreement will terminate automatically on the date of filing such voluntary or involuntary petition in bankruptcy.

7.5On any termination of this Agreement, LICENSEE and/or its AFFILIATES or SUBLICENSEES shall have the right to continue to sell out all remaining stocks of LICENSED PRODUCTS under the terms and conditions of this Agreement, provided LICENSEE pays LICENSOR the royalties due and payable on NET SALES of such LICENSED PRODUCTS as provided for herein.

7.6In the event LICENSEE allows the insurance coverage that is required to be maintained under Section 9.6 to lapse, LICENSEE must notify LICENSOR in writing as soon as practicable. If LICENSEE fails to notify LICENSOR of such lapse within three (3) business days, this Agreement and the licenses granted herein shall immediately and automatically terminate without notice. Upon such notification by LICENSEE to LICENSOR, LICENSEE will have thirty (30) business days to correct such lapse by obtaining the required insurance. If LICENSEE fails to correct such lapse in thirty (30) business days, this Agreement and the licenses granted herein shall immediately and automatically terminate without notice.
Upon termination of this Agreement as provided for in this Section 7.6, LICENSEE shall have the right to reinstate the effectiveness of this Agreement by obtaining the required insurance, whereupon this Agreement shall automatically become effective as of the date of reinstatement of said insurance, and shall remain in full force and effect without any further action of the parties hereto until termination or expiration of this Agreement according to Sections 7.1, 7.2, 7.3 or 7.4.

7.7 Surviving any termination or expiration are:

a. LICENSEE's obligation to pay royalties and fees accrued as of the effective date of any termination or expiration or accruing under Section 7.5;

b. Any cause of action or claim of LICENSEE or LICENSOR, accrued as of the effective date of any termination or expiration, because of any breach or default by the other party; and

c. The provisions of Sections 5.3, 7.1, 7.5, 7.6, 7.7, 7.8,7.9, 8.4, 9.5, 9.6, 9.7, 9.10. 9.11, 9.19, 9.20 and 9.21.

7.8 No relaxation, forbearance, delay or indulgence by either party in enforcing any of the terms of this Agreement or the granting of time by either party to the other shall prejudice, affect or restrict the rights and powers of the former hereunder nor shall any waiver by either party of a breach of this Agreement be considered as a waiver of any subsequent breach of the same or any other provision hereof.

7.9 LICENSOR's exercise of the right to terminate this Agreement under this Article VII as a result of LICENSEE's failure to meet any of the diligence requirements under Sections 4.1 or 4.2, shall be LICENSOR's sole and exclusive remedy, and LICENSEE's sole and exclusive liability, for LICENSEE's failure to meet any of the diligence requirements under Sections 4.1 or 4.2.

VIII. SUBLICENSE(S)

8.1 LICENSEE shall have the right to seek SUBLICENSES subject to the terms and conditions of this Agreement as stated in Article II and as defined in this Article VIII. AFFILIATES shall have no licenses under the LICENSED PATENT RIGHTS unless such AFFILIATES are granted a SUBLICENSE. All SUBLICENSES will be consistent with and subject to the applicable terms and conditions of this Agreement. SUBLICENSEES shall have the right to further SUBLICENSE. For the purposes of this Agreement, the LICENSEE shall be responsible to LICENSOR for the acts and omissions of its SUBLICENSEES, including its SUBLICENSEES' compliance with the applicable terms and conditions of this Agreement. Moreover, it is understood and agreed that if an AFFILIATE or a SUBLICENSEE meets or fulfills any or all of the obligations of LICENSEE under this Agreement, and/or observes any of the terms or conditions hereof, then LICENSEE shall be deemed to have met or fulfilled such obligations or observed such terms or conditions, as the case may be. In addition to payment of royalties on NET SALES, LICENSEE will pay to LICENSOR a percentage, as specified in Appendix B, subsection 3, of SUBLICENSING REVENUES.

8.2 If LICENSEE licenses to a third party patent rights that have been licensed or assigned to, or otherwise acquired by, LICENSEE other than under this Agreement ("LICENSEE's Patent Rights"), and LICENSEE believes, in good faith, that such third party will infringe LICENSED PATENT RIGHTS in practicing the LICENSEE's Patent Rights, then LICENSEE will not separately grant a license to such third party under LICENSEE's Patent Rights without concurrently granting a SUBLICENSE under LICENSED PATENT RIGHTS. In such event, if LICENSEE receives any SUBLICENSING REVENUES as a result of such grant of a license under LICENSEE's Patent Rights, and a grant of a SUBLICENSE under LICENSED PATENT RIGHTS, then LICENSEE shall be obligated to pay LICENSOR a percentage of such SUBLICENSING REVENUES as provided for in Appendix B, subsection 3. In the event that LICENSOR and LICENSEE each owns an undivided one half interest in any LICENSED PATENT RIGHTS ("Joint Patents"), LICENSEE may separately grant a license to any third party under its rights to Joint Patents without the consent of LICENSOR, provided any such license concurrently grants a SUBLICENSE under LICENSOR's rights on the terms and conditions described in this Article VIII. LICENSOR shall not grant a license to any third party under any Joint Patents, or grant any third party the right to use, practice or otherwise exploit any Joint Patents. Joint Patents shall be added to Appendix A and deemed and treated as part of the LICENSED PATENT RIGHTS.

8.3 The LICENSEE will notify LICENSOR of each SUBLICENSE granted hereunder and provide LICENSOR with a redacted copy of each SUBLICENSE within thirty (30) days of the grant of the SUBLICENSE. No portion of such SUBLICENSE relevant to this Agreement will be redacted.

8.4 Upon termination of this Agreement for any reason, any or all SUBLICENSES will remain in full force and effect at the sole discretion of the SUBLICENSEES, and will be assigned to LICENSOR such that such SUBLICENSEES are in direct privity with LICENSOR; provided, however, that each such SUBLICENSEE is in material compliance with the applicable provisions of this Agreement as of the effective date of such termination and agrees in writing to assume and be bound by all of the obligations of LICENSEE under this Agreement that are applicable to such SUBLICENSEE. In the event of termination of this Agreement and such assignment of any SUBLICENSE, LICENSOR will not be bound by any grant of rights broader than, nor will it be required to perform any obligation other than, those rights and obligations contained in this Agreement. Moreover, pursuant to such assignment, LICENSOR will have the sole right to modify each such assigned SUBLICENSE but only to include rights of LICENSOR that are contained in this Agreement, including the payment of royalties directly to

LICENSOR and Annual Minimum Payments and Milestone Payments per Appendix B, and reimbursement of Patent Prosecution Costs per Sections 4.4 through 4.8.

IX. MISCELLANEOUS

9.1 Nothing in this Agreement shall create, or be deemed to create, a partnership, or the relationship of principal and agent, between the parties.

9.2Assignment. So long as LICENSEE is not in material breach of this Agreement, LICENSEE may assign or otherwise transfer this Agreement and/or the rights acquired by it hereunder upon obtaining consent from the LICENSOR for the same (such consent will not be unreasonably withheld, delayed or conditioned such as upon additional consideration). However, LICENSEE shall be free to assign this Agreement or otherwise transfer its rights or obligations under this Agreement, to an AFFILIATE, by operation of law pursuant to an acquisition, merger, sale of stock or assets or consolidation of LICENSEE with or into a third party, or upon the transfer or sale of all or substantially all of the business or assets to which this Agreement pertains, in each case without obtaining any consent from LICENSOR. LICENSEE shall give the LICENSOR written notice of LICENSEE's assignment or transfer of this Agreement within thirty (30) days after completion of such assignment or transfer, along with a redacted copy of such assignment agreement, pursuant to which such assignee or transferee shall have agreed in writing to be bound by the terms and conditions of this Agreement. No portion of such assignment agreement relevant to this Agreement will be redacted. Upon completion of such assignment or transfer, the term "LICENSEE" as used herein shall refer to such assignee or transferee. If LICENSEE shall sell or otherwise transfer its entire business, and the transferee shall not have agreed in writing to be bound by the terms and conditions of this Agreement, within sixty (60) days of such sale or transfer, the LICENSOR shall have the right to terminate this Agreement upon thirty (30) days written notice to LICENSEE if such transferee does not agree in writing to be bound by the terms and conditions of this Agreement within such thirty (30) day period.

9.3 Section left intentionally blank.

9.4 LICENSEE shall provide appropriate patent notices on all finished, packaged LICENSED PRODUCTS and/or provide for appropriate virtual marking on finished, packaged LICENSED PRODUCTS as specified in the patent and other statutes, and will require all SUBLICENSEES and/or AFFILIATES to do the same.

9.5 To the extent permitted by law, each party assumes all risks of personal injury, bodily injury including death, and property damage to the extent caused by the negligent acts or omissions of that party. LICENSEE shall at all times during the term of this Agreement and thereafter indemnify, defend and hold LICENSOR, VCU and VA, its trustees, directors, officers, employees and affiliates (collectively, "Indemnitees") harmless against all third party claims, proceedings, demands and liabilities, including legal expenses (collectively, "Liabilities") arising out of the death of or injury to any person or persons or out of any damages to property to the extent resulting from the research, development, production, manufacture, sale, modification, use, import or advertisement of LICENSED PRODUCTS by or on behalf of LICENSEE or its AFFILIATES or SUBLICENSEES, or to the extent resulting from LICENSEE or its AFFILIATES or SUBLICENSEES carrying out any obligation of LICENSEE hereunder. LICENSEE's obligations under this Section 9.5 shall not apply with respect to any Liabilities that are due to the gross negligence of, or willful misconduct by, any Indemnitee or VCU/ VA Personnel. LICENSEE's indemnification obligations under this Agreement shall in any event be conditioned upon the following: (i) the indemnified party shall provide LICENSEE with prompt written notification of any claim for which indemnity is sought; (ii) the indemnified party shall cooperate with and permit

LICENSEE to assume full control of the defense and settlement of such claim; and (iii) the indemnified party shall not agree to dispose of or settle any such claim without the prior written consent of LICENSEE.

9.6 LICENSEE shall obtain and carry in full force and effect during the term hereof and for a period of five (5) years after any termination or expiration, commercial, general liability insurance. Such insurance shall be written by a reputable company authorized to do business in the Commonwealth of Virginia, shall list LICENSOR, VCU and VA as an additional insured thereunder, shall be endorsed to include LICENSED PRODUCTS liability coverage and shall require reasonable written notice to be given to LICENSOR prior to any cancellation or material change thereof. The limits of such insurance shall not be less than one million dollars ($1,000,000) per occurrence with an aggregate of five million ($5,000,000) for personal injury or death, and one million dollars ($1,000,000) per occurrence with aggregate of three million dollars ($3,000,000) for property damage. LICENSEE shall provide LICENSOR with Certificates of Insurance evidencing same.

9.7Limitation on Liability. LICENSEE shall not be liable to LICENSOR, VA or VCU for any special, indirect, incidental, punitive or consequential damages (including without limitation, damages resulting from loss of use, loss of profits, interruption or loss of business or other economic loss) arising out of this Agreement or with respect to LICENSEE's performance or non-performance hereunder, even if LICENSEE knew or should have known of the possibility of such damages.

9.8Representations and Warranties; Disclaimers.

(a) LICENSOR REPRESENTS AND WARRANTS ON BEHALF OF ITSELF, VCU AND VA, IN ACCORDANCE WITH THE IIA, THAT IT OR VCU IS THE SOLE OR JOINT OWNER (WITH THE VA) OF THE LICENSED TECHNOLOGY AND LICENSED PATENT RIGHTS AND IT HAS THE RIGHT TO GRANT THE EXCLUSIVE RIGHTS AND LICENSES THAT ARE GRANTED HEREUNDER AND CONTEMPLATED TO BE GRANTED HEREUNDER, BY AND ON BEHALF OF ITSELF, VCU, THE VA AND THE INVENTOR(S) AND NON-INVENTOR(S).

(b) LICENSOR REPRESENTS (I) TO THE BEST OF ITS KNOWLEDGE THERE IS NO PENDING OR THREATENED CLAIM, LITIGATION, INQUIRY, INVESTIGATION OR PROCEEDING WHICH COULD HAVE AN ADVERSE EFFECT ON ANY OF THE LICENSED TECHNOLOGY OR LICENSED PATENT RIGHTS, THIS AGREEMENT OR LICENSOR'S ABILITY TO MEET ITS OBLIGATIONS HEREUNDER OR OBSERVE THE TERMS AND CONDITIONS HEREOF; (II) TO THE BEST OF ITS KNOWLEDGE THERE IS NO AGREEMENT TO WHICH LICENSOR, VCU OR VA IS A PARTY OR BY WHICH IT IS BOUND THAT PROHIBITS OR WOULD PROHIBIT THE EXECUTION AND DELIVERY OF THIS AGREEMENT OR THE PERFORMANCE OR FULFILLMENT BY ANY OF THEM OF ANY OBLIGATION OR THE OBSERVANCE OF ANY TERM OR CONDITION HEREIN AND NEITHER LICENSOR, VCU NOR VA SHALL ENTER INTO ANY SUCH AGREEMENT DURING THE TERM HEREOF, (III) TO THE BEST OF ITS KNOWLEDGE, ON THE EFFECTIVE DATE OF THIS AGREEMENT, OTHER THAN UNITED STATES GOVERNMENT GRANTS SPONSORING RESEARCH OF DR. SHUNLIN REN OR ANY OTHER INVENTOR, THERE ARE NO PRE-EXISTING THIRD PARTY OBLIGATIONS ON THE PART OF LICENSOR, VCU OR VA, INCLUDING UNDER ANY SPONSORED RESEARCH AGREEMENTS, INVOLVING DR. SHUNLIN REN OR ANY OTHER INVENTOR, THAT RELATE TO ANY OF THE LICENSED TECHNOLOGY, AND (IV) UPON EFFECTIVE DATE, DR. SHUNLIN REN IS A DAP (AS DEFINED IN THE IIA).

(C) EXCEPT TO THE EXTENT EXPRESSLY PROVIDED FOR IN THIS AGREEMENT, NOTHING IN THIS AGREEMENT SHALL BE CONSTRUED AS (I) A WARRANTY OR

REPRESENTATION BY LICENSOR AS TO THE VALIDITY OR SCOPE OF ANY LICENSED PATENT RIGHTS, (II) A WARRANTY OR REPRESENTATION THAT ANYTHING MADE, USED, IMPORTED, DEVELOPED, PROMOTED, OFFERED FOR SALE, SOLD, OR OTHERWISE DISPOSED OF UNDER ANY LICENSE GRANTED IN THIS AGREEMENT DOES NOT OR WILL NOT INFRINGE PATENTS, TRADE SECRETS OR OTHER PROPRIETARY RIGHTS OF THIRD PARTIES; (III) AN OBLIGATION TO BRING OR PROSECUTE ACTIONS OR SUITS AGAINST THIRD PARTIES FOR INFRINGEMENT; (IV) CONFERRING THE RIGHT TO USE IN ADVERTISING, PUBLICITY OR OTHERWISE ANY TRADEMARK, TRADE NAME, OR NAMES, OR ANY CONTRACTION, ABBREVIATION, SIMULATION OR ADAPTATION THEREOF OF VCU, VA OR LICENSOR; (V) CONFERRING BY IMPLICATION, ESTOPPEL OR OTHERWISE ANY LICENSE OR RIGHTS UNDER ANY PATENTS OF LICENSOR OTHER THAN THE LICENSED PATENT RIGHTS; (VI) ANY OTHER REPRESENTATIONS OR WARRANTIES, EITHER EXPRESS OR IMPLIED, UNLESS SPECIFIED IN THIS AGREEMENT; (VII) DIRECTLY OR INDIRECTLY OPERATING OR APPLYING AS A WAIVER OF SOVEREIGN IMMUNITY BY THE COMMONWEALTH OF VIRGINIA; OR (VIII) IMPOSING ANY OBLIGATION OR ANY LIABILITY ON ANY PARTY CONTRARY TO THE LAWS OF THE COMMONWEALTH OF VIRGINIA. LICENSOR DISCLAIMS AND MAKES NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE WITH RESPECT TO THE LICENSED RIGHTS, OR ANY LICENSED PRODUCTS.

(d) OTHER THAN AS EXPRESSLY PROVIDED FOR IN THIS AGREEMENT, LICENSEE MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OR GUARANTEES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION, THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OR GUARANTEES THAT LICENSEE OR ANY AFFILIATE OR SUBLICENSEE WILL SUCCESSFULLY DEVELOP, REGISTER, OBTAIN REGULATORY APPROVAL FOR, MANUFACTURE OR COMMERCIALIZE ANY LICENSED PRODUCTS, OR THAT ANY LICENSED PRODUCT WILL BE MERCHANTABLE, FIT FOR ITS INTENDED PURPOSE OR WILL NOT INFRINGE OR MISAPPROPRIATE THE INTELLECTUAL PROPERTY RIGHTS OF ANY PERSON OR ENTITY.

9.9 For the purposes of this Agreement "Force Majeure" means any circumstances beyond the reasonable control of either party including, without limitation, any strike, lock-out, labor dispute or other form of industrial action, acts of God, acts of government (including injunctions), fire, flood, earthquake, breakdown of plant, damage to or loss, shortage or unavailability of equipment, facilities or materials, failure of suppliers, unavailability of utilities, common carriers or manufacturing, casualty or accident, civil commotion, acts of public enemies, acts of terrorism or threat of terrorist acts, blockage or embargo and the like. If either party is affected by Force Majeure, it shall forthwith notify the other party of the nature and extent thereof. Neither party shall be deemed to be in breach of this Agreement, or otherwise be liable to the other, by reason of any delay in performance, or the non-performance, of any of its obligations under this Agreement, to the extent that such delay or non-performance is due to any Force Majeure of which it has notified the other party, and the time for performance of that obligation shall be extended accordingly. If the Force Majeure in question prevails for a continuous period in excess of six (6) months, the parties shall enter into bona fide discussions with a view to alleviating its effects, or to agreeing upon such alternative arrangements as may be fair and reasonable.

9.10 LICENSEE shall not use the names or trademarks of LICENSOR, nor any adaptation thereof, nor the names of any of its employees, in any advertising, promotional or sales literature without prior written consent obtained from LICENSOR, or said employee, in each case, except that the LICENSEE may state

that it is a LICENSEE of LICENSOR with respect to the LICENSED TECHNOLOGY and/or LICENSED PATENT RIGHTS.

9.11 Any notice or payment required to be given to either party will be deemed to have been properly given and to be effective:

a. on the date of delivery if delivered in person;
b. on the date of mailing if mailed by first-class certified mail, postage paid; or
c. on the date of mailing if mailed by any global express carrier service that requires the recipient to sign the documents demonstrating the delivery of such notice or payment;

to the respective addresses given below, or to another address as designated in writing by the party changing its address.

VIRGINIA COMMONWEALTH UNIVERSITY
INTELLECTUAL PROPERTY FOUNDATION

President
Box 980568
800 E. Leigh Street, Suite 113
Virginia Commonwealth University
Richmond, VA 23298-0568

DURECT CORPORATION
Attn: Legal Department
DURECT Corporation
10260 Bubb Road
Cupertino, CA 95014

9.12 This Agreement contains the entire and only agreement and understanding between the parties and supersedes all preexisting and contemporaneous agreements, including the Option Agreement, between them respecting its subject matter. The SRA, the Bilateral Confidentiality Agreement between LICENSEE and VCU dated December 1, 2011 (the “CDA”) and the Outgoing Materials Transfer Agreement between LICENSEE and VCU dated January 6, 2012 shall continue in full force and effect in accordance with their terms. Any representation, promises, or condition in connection with such subject matter which is not incorporated in this Agreement shall not be binding on either party. No modification, renewal, waiver, and no termination of this Agreement or any of its provisions shall be binding upon the party against whom enforcement of such modification, renewal, waiver or termination is sought, unless made in writing and signed on behalf of such party by one of its duly authorized officers. As used herein: the word "termination" includes any and all means of bringing an end prior to its expiration by its own terms this Agreement, or any provisions thereof, whether by release, discharge, abandonment or otherwise. This Agreement may not be amended except by written agreement of the parties.

9.13 This Agreement shall be construed, governed, interpreted and applied in accordance with the laws of the Commonwealth of Virginia, U.S.A., except that questions affecting the construction and effect of any patent shall be determined by the law of the country in which the patent was granted. Any legal action or proceeding relating to this Agreement or any document or instrument related hereto shall be

brought only in the courts of the Commonwealth of Virginia in Richmond, Virginia, and by its execution and delivery of this Agreement, LICENSEE hereby accepts for itself and in respect to its property, generally and unconditionally, the jurisdiction of the aforesaid courts.

9.14 This Agreement may be executed in one or more counterparts and any party hereto may execute any such counterparts each of which shall be deemed an original and all of which, taken together, shall constitute but one and the same document. It shall not be necessary in making proof of this document or any counterpart hereof to produce or account for any of the other counterparts.

9.15 The provisions of this Agreement are severable, and in the event that any provisions of this Agreement shall be determined to be invalid or unenforceable under any controlling body of the law, such invalidity and unenforceability shall not in any way affect the validity or enforceability of the remaining provisions hereof. In the event the validity or unenforceability of any provision of this Agreement is brought into question because of the decision of a court of competent jurisdiction, the parties by mutual written agreement may revise the provision in question or may delete it entirely so as to comply with the decision of said court.

9.16 The failure of either party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement shall not constitute a waiver of that right or excuse a similar failure to perform any such term or condition by the other party.

9.17 It is understood that LICENSOR and VCU are subject to United States laws and regulations controlling the export of technical data, computer software, laboratory prototypes and other commodities (including the Arms Export Control Act, as amended and the United States Department of Commerce Export Administration Act of 1979). The transfer of such items may require a license from the appropriate agency of the United States Government and/or written assurances by LICENSEE that LICENSEE shall not export data or commodities to certain foreign countries without prior approval of such agency. LICENSOR neither represents that license shall not be required nor, if required, it shall be issued.

9.18 All reports and documents to be forwarded to LICENSOR shall be in the English language.

9.19 Proprietary Information.

(a) Each party solely owns its Proprietary Information. Each party shall treat Proprietary Information received from the other party with the same degree of care with which it treats its own Proprietary Information, but in any event no less than a reasonable degree of care, and further agrees not to disclose such Proprietary Information to a third party without prior written consent from the party disclosing Proprietary Information. Notwithstanding the foregoing, LICENSEE may disclose the existence and terms of this Agreement and the Proprietary Information of LICENSOR, VA or VCU to: (i) LICENSEE's employees, agents and contractors on a need to know basis for the purpose of LICENSEE performing its obligations and exercising its rights under this Agreement, including without limitation, those persons and entities involved in research, development, manufacturing, marketing, promotion, distribution, sale and/or commercialization of LICENSED PRODUCTS, LICENSED TECHNOLOGY and/or LICENSED PATENT RIGHTS, and (ii) its AFFILIATES and actual and potential acquirers, investors, assignees, transferees, licensees (including SUBLICENSEES) and other business partners, in each case under conditions of confidentiality. LICENSOR may disclose this Agreement and the Proprietary Information of LICENSEE to the VA in accordance with the IIA; provided that LICENSOR (i) only submits to the VA the Proprietary Information of LICENSEE that is necessary to meet the requirements under Article 5.2 of the IIA, (ii) labels any and all Proprietary Information of LICENSEE as

"confidential" and takes whatever measures are otherwise required in order for Proprietary Information of LICENSEE to be received and treated by VA as confidential under the IIA, and (iii) in instances in which LICENSOR is aware, gives LICENSEE prior written notice of VA's disclosure of any Proprietary Information of LICENSEE as required by law, court order or regulation and an opportunity to participate in drafting a protective order or otherwise limiting the disclosure to the extent possible.

(b) Proprietary Information of LICENSEE shall include without limitation, any information of LICENSEE or its AFFILIATES or SUBLICENSEES that is furnished or otherwise made available to LICENSOR or its representatives under Article V including progress reports and royalty reports, and any and all other information, data, and materials in whatever form relating to LICENSEE's products (including but not limited to LICENSED PRODUCTS), technologies (including but not limited to processes, methods, procedures, techniques, formulas, formulations, algorithms, programs, designs, drawings, devices, engineering, manufacturing, equipment or facilities) or business (including but not limited to research and development and results thereof, preclinical, clinical, regulatory, sales and marketing plans and strategies, financings, business development, personnel, present and future products, vendors and suppliers, customers, SUBLICENSEES, intellectual properties and confidential information of third parties). For clarity, Proprietary Information of LICENSEE also includes any and all data, results, reports and analyses arising from the testing of LICENSED PRODUCTS by LICENSEE, its AFFILIATES or SUBLICENSEES or on behalf of LICENSEE, its AFFILIATES or SUBLICENSEES by a third party, including without limitation, as a result of any animal studies, toxicological testing or human clinical testing; provided, however, that LICENSEE's rights with respect to any such data, results, reports and analyses that are generated under the SRA shall be subject to the terms and conditions of the SRA, in particular and without limitation, the right to publish any and all such data and results produced by VCU/VA Personnel in accordance with the terms of the SRA. The parties may disclose the existence of this Agreement, but the unpublished patent applications and invention disclosures in Appendix A and the terms and conditions described in Section 4.2 and Appendix B of this Agreement shall be the Proprietary Information of both parties and shall not be used or disclosed other than as provided for in this Section 9.19. Notwithstanding the foregoing, the information disclosed under Section 8.3 and Article V of this Agreement shall be the Proprietary Information of LICENSEE and shall not be used or disclosed by LICENSOR other than as provided for in this Section 9.19.

(c) Neither party shall use the Proprietary Information of the other party other than in performing its obligations or exercising its rights under this Agreement which, in the case of LICENSEE shall include without limitation, in connection with LICENSEE's preparation and filing of regulatory submissions with regulatory authorities, design and conduct of clinical trials, and obtaining and/or maintaining regulatory approvals for LICENSED PRODUCTS.

(d) The foregoing obligations of non-disclosure and non-use do not apply to Proprietary Information which: (i) was known to the recipient (or in the case of LICENSEE, its AFFILIATES or SUBLICENSEES) prior to the disclosure hereunder as shown by the recipient's (or its AFFILIATES' or SUBLICENSEES') prior written records; (ii) was received by recipient (or in the case of LICENSEE, its AFFILIATES or SUBLICENSEES) from a third party not under an obligation of confidence to the discloser; (iii) is in the public domain at the time of disclosure hereunder or subsequently entered the public domain without the fault of the recipient or anyone to whom the recipient disclosed the Proprietary Information; or (iv) has been independently developed by an employee of recipient (or in the case of LICENSEE, its AFFILIATES or SUBLICENSEES) who has not had knowledge of or access directly or indirectly to Proprietary Information, and recipient or its AFFILIATES or SUBLICENSEES can substantiate any claim of

independent development by written evidence; or (v) is approved for release by written authorization of the discloser.

(e) Unless otherwise agreed to in writing by the parties, the parties shall be subject to the confidentiality, non-disclosure and non-use obligations hereunder with respect to the Proprietary Information of the other party during the term hereof and for a period of five (5) years following the expiration or earlier termination of this Agreement.

(f) A recipient of Proprietary Information may disclose that portion of the other party's Proprietary Information if and to the extent recipient is required to make such disclosure pursuant to law or governmental regulation or to any governmental entity having jurisdiction (including a court of competent jurisdiction), provided recipient promptly notifies the other party in writing as soon as reasonably practical or possible, prior to such disclosure, of the receipt of such request, and takes reasonable and lawful actions to avoid and/or minimize the extent of such disclosure and seeks to obtain confidential treatment based on advice of their legal counsel or provides assistance to the other party in obtaining a protective order therefor if reasonably requested by the other party. For the avoidance of doubt, this Section 9.19(f) shall also apply with respect to any Freedom of Information Act (FOIA) requests that may be made with respect to this Agreement including any of its Appendices, or any other Proprietary Information of LICENSEE. To the extent permitted by law, LICENSOR agrees to redact any enabling titles of any unpublished patent applications (as well as such unpublished patent applications) listed in Appendix A, and Appendix B, from any disclosures required to be made under law or regulation or by any court, including under FOIA, and to allow LICENSEE to review, in advance of any such disclosure, the proposed disclosure and to take into account in good faith any comments that LICENSEE may provide with respect to such proposed disclosure.

(g) Notwithstanding the foregoing or anything to the contrary herein, LICENSEE and its AFFILIATES and SUBLICENSEES may disclose Proprietary Information if required by (i) laws, rules or regulations of a securities exchange or other government agency, such as the Securities and Exchange Commission, (ii) a governmental authority or agency for purposes of obtaining or maintaining approval to test or market a LICENSED PRODUCT, or (iii) a patent office for the purposes of filing, prosecuting or otherwise obtaining or maintaining intellectual property rights. In addition to the foregoing, LICENSEE and its AFFILIATES and SUBLICENSEES may disclose the terms of this Agreement in footnotes to their financial statements, to the extent required under generally accepted accounting principles.

(h) Upon any termination or expiration of this Agreement, each party shall promptly return to the other party (or destroy at the other party's written election) any and all Proprietary Information of the other party (including copies, summaries, excerpts, extracts or other reproductions and embodiments thereof) in any form including electronic form (including electronic media such as DVD, CD-ROM, electronic copies or any material resident in the hard or external drive of any computer), and any other materials otherwise containing or reflecting any Proprietary Information of the other party that is in such party's possession, custody or control. Notwithstanding the foregoing, each party may retain one (1) copy of the other party's Proprietary Information for the sole purposes of monitoring its ongoing obligations hereunder.

(i) The parties may disclose the existence of this Agreement which, in the case of LICENSOR, shall be limited to disclosure to the extent required by VCU policies and further limited to describing in general terms the LICENSED TECHNOLOGY and LICENSED PATENT RIGHTS as follows: the name and number of any published patent application or patent that is included in the

LICENSED PATENT RIGHTS, non-enabling titles of any unpublished patent applications listed in Appendix A and the fact that the LICENSED PATENT RIGHTS have been licensed to LICENSEE. LICENSOR shall notify LICENSEE in writing in advance of any required disclosure of the existence of this Agreement and/or description of the LICENSED TECHNOLOGY or LICENSED PATENT RIGHTS, which in each case shall be subject to LICENSEE's review and comment.

9.20 Publications. LICENSOR agrees not to publish, present or otherwise disclose any Proprietary Information of LICENSEE. LICENSEE shall be furnished copies of any proposed disclosure, publication or presentation (including any modifications thereof which LICENSEE has not yet reviewed) containing or referring to any LICENSED TECHNOLOGY or LICENSED PATENT RIGHTS at least thirty (30) days before submission of such proposed disclosure, publication or presentation. With regard specifically to modification(s) to a disclosure, publication or presentation that LICENSEE has already reviewed prior to such modification(s), LICENSOR agrees that any Proprietary Information of LICENSEE which has been identified in writing by LICENSEE shall be deleted from the disclosure, publication or presentation and LICENSOR shall send LICENSEE a statement verifying that this has been done along with a final copy including the revision. In no event shall LICENSEE's review of any modification to a disclosure, publication or presentation exceed the original 30 day review period unless LICENSEE requests delay for patent protection. During its review period(s), LICENSEE shall have the right to review the material for Proprietary Information of LICENSEE and to assess the patentability of any invention described in the material. If LICENSEE decides that a patent application should be filed, the disclosure, publication or presentation shall be delayed an additional sixty (60) days or a shorter period of time if LICENSEE consents in writing, whichever is sooner. At LICENSEE's written request, Proprietary Information of LICENSEE shall be deleted. For the avoidance of doubt, proposed disclosures from LICENSOR to VCU shall be deemed and treated as proposed disclosures for the purposes hereof. Although LICENSEE shall have the option not to include its name on any publication or presentation, at LICENSEE's request, any disclosure, publication or presentation made by LICENSOR and relating to LICENSED TECHNOLOGY or LICENSED PATENT RIGHTS shall acknowledge LICENSEE's contribution thereto in accordance with customary scientific practice.

9.21 Further Actions. Each party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

[SIGNATURES APPEAR ON NEXT PAGE]

IN WITNESS WHEREOF, the parties have caused this Agreement to be executed in duplicate as first above written.

AGREED AND ACCEPTED:

DURECT CORPORATION:

By: /s/ James E. Brown Date: Dec. 5, 2012
Title C.E.O.

VIRGINIA COMMONWEALTH UNIVERSITY
INTELLECTUAL PROPERTY FOUNDATION

By: /s/ Ivelina S. Metcheva Date: 12/5/12
Ivelina S. Metcheva, Ph.D., MBA
Director, VCU Office of Technology Transfer
President VCU Intellectual Property Foundation

APPENDIX A
LICENSED PATENT RIGHTS

U.S. Patent Application:

Provisional Serial No. 60/621,537, filed October 25, 2004	Nuclear Oxysterol, Potent Regulator Of Cholesterol Homeostasis, For Therapy Of Hypercholesterolemia, Hyperlipidemia, and Atherosclerosis
Non-Provisional Serial No. 11/739,330, filed April 26, 2007	Nuclear Sulfated Oxysterol, Potent Regulator Of Cholesterol Homeostasis, For Therapy Of Hypercholesterolemia, Hyperlipidemia, and Atherosclerosis
Provisional Serial No. 61/154,063, filed February 20, 2009	5-Cholesten-3b , 25-diol 3-sulfate (25HC3S), an authentic PPARy agonist and LXR antagonist, or the therapy of inflammatory diseases
Non-Provisional Serial No. 12/708,803, filed February 19, 2010	Nuclear Sulfated Oxysterol, Potent Regulator Of Lipid Homeostasis, For Therapy Of Hypercholesterolemia, Hypertriglycerides, Fatty Liver Diseases, and Atherosclerosis
Provisional Serial No. 61/472,293, filed April 6, 2011	Hydroxysteroid sulfotransferase (SULT2B1b) for therapy of hyperlipidemia and fatty liver diseases
Non-Provisional, Serial No. 13/441,241, filed April 6, 2012	Sulfated Oxysterol and Oxysterol Sulfation by Hydroxysterol Sulfotransferase Promote Lipid Horneostasis and Liver Proliferation
Provisional Serial No. 61/604,711, filed February 29, 2012	Sulfated oxysterol, 25HC3S and oxysterol sulfation by hydroxysterol sulfotransferase (SULT2Blb) promote liver proliferation: therapy for cirrhosis, injury, recovery following hepatectomy, and other applications
Provisional Serial No. 61/623,203, filed April 12, 2012 Provisional Serial No. 61/623,414, filed April 12, 2012	A Novel Cholesterol Metabolite, 5-Cholesten, 3-,25-diol, Disulfate (25HCDS) for Therapy of Metabolic Disorders, Hyperlipidemia, Fatty Liver Disease, Diabetes and Atherosclerosis

VCU Invention Disclosures

VCU Invention Disclosure No.	**Title**
REN-04-072, disclosed September 24, 2004	Nuclear oxysterol, potent regulator of cholesterol hemeostasis, for therapy of hypercholesterolemia, hyperlipidemia, and atherosclerosis
REN-08-078, disclosed December 15, 2008	5-Cholesten-3b, 25-diol 3-sulfate (25HC3S), an authentic PPARy agonist and LXR antagonist, for the therapy of inflammatory diseases, such as inflammatory bowel diseases, fat liver diseases, and atheroclerotic diseases
REN-11-030, disclosed April 5, 2011	Hydroxysteroid sulfotransferase (SULT2B1b) for therapy of hyperlipidemia and fatty liver diseases

REN-11-93, disclosed November 7, 2011	Sulfated oxysterols, 25HC3S and 25HCDS, and oxysterol sulfation by hydroxysterol sulfotransferase (SULT2B1b) promote liver proliferation: therapy for cirrhosis, injury, and recovery following hepatectomy
REN-11-94, disclosed November 7, 2011	A novel cholesterol metabolite, 5-cholesten, 3-,25-diol, disulfate (25HCDS) for therapy of metabolic disorders, hyperlipidemia, diabetes, fat liver diseases, and atherosclerosis
REN-12-025, disclosed March 26, 2012	A Novel Cholesterol Metabolite, 5-Cholesten, 3-,25-diol, Disulfate (25HCDS) for Therapy of Metabolic Disorders, Hyperlipidemia, Diabetes, Fat Liver Diseases, and Atherosclerosis
REN-12-061, disclosed June 21, 2012	Novel Oxysterol, 5-Cholesten 3,27-diol 27-Glucuronide, for Therapy of Hypertriglyceridemia
REN-12-075	Low Levels of Oxysterol Sulfates, 25-,24, and 27(26)-hydroxycholesterol Sulfates, as biomarkers for diagnosis of lipid metabolic disorders, nonalcoholic fatty liver diseases

APPENDIX B
FEES AND ROYALTIES

1. LICENSEE agrees to pay LICENSOR a noncreditable, nonrefundable one time only License Issue Fee of one-hundred thousand dollars ($100,000.00) within ten (10) days of the full execution and delivery of this Agreement. Subject to Sections 4.4 through 4.9, LICENSEE also agrees to reimburse to LICENSOR all documented Patent Prosecution Costs not already reimbursed by LICENSEE for LICENSED PATENT RIGHTS incurred prior to and during the term of this Agreement within thirty (30) days of receipt of an undisputed invoice from LICENSOR.

2. Royalty rate:

a. LICENSEE agrees to pay to LICENSOR a running royalty of two percent (2%) of NET SALES of LICENSED PRODUCTS sold by LICENSEE, its AFFILIATES or any SUBLICENSEE in a country where, and for so long as, the manufacture, use, or sale of such LICENSED PRODUCTS is covered by a VALID CLAIM of LICENSED PATENT RIGHTS in such country of sale.

b. LICENSEE agrees to pay to LICENSOR a running royalty of one percent (1%) of NET SALES of LICENSED PRODUCTS made by LICENSEE, its AFFILIATES or any SUBLICENSEE in a country where, and for so long as, the manufacture or production of such LICENSED PRODUCTS is covered by a VALID CLAIM of LICENSED PATENT RIGHTS in such country, and sold in a country where the manufacture, use or sale of such LICENSED PRODUCTS is not covered by a VALID CLAIM of LICENSED PATENT RIGHTS in such country of sale. This one percent (1%) rate will not be reduced by the royalty stacking clause described in subsection (d) below.

c. For clarity, LICENSEE shall pay LICENSOR only one royalty with respect to the same unit of LICENSED PRODUCT made, used, imported or sold, regardless of the number of VALID CLAIMS of the LICENSED PATENT RIGHTS or number of LICENSED PATENT RIGHTS covering such LICENSED PRODUCT or its manufacture, use, import or sale.

d. In the event that the LICENSEE's royalty obligation to LICENSOR combined with any third-party obligations is equal to or greater than a threshold cumulative royalty (TCR) of four percent (4.0 %), the royalty payable (R1) by LICENSEE to the LICENSOR will be reduced by an amount proportionate to the amount by which the total royalty paid by the LICENSEE exceeds the threshold as follows:

$$R2 = R1(1-[T- TCR]/T),$$

where T is the total cumulative royalty the LICENSEE must pay on LICENSED PRODUCTS requiring third-party licenses (which total cumulative royalty includes the royalty to be paid to LICENSOR hereunder) and R2 is the adjusted royalty to be paid to the LICENSOR. Notwithstanding the foregoing, the royalty due to the LICENSOR will not be reduced by more than fifty percent (50%).

e. If LICENSEE or any AFFILIATE or SUBLICENSEE is required to withhold a tax from any royalty or other payment due to LICENSOR hereunder, LICENSEE or such AFFILIATE or SUBLICENSEE shall deduct from such royalty or other payment the tax amount to be withheld, and shall furnish LICENSOR with a copy of any tax certificate or other documentation evidencing such withholding. However, where appropriate, LICENSEE shall give LICENSOR appropriate notice to allow LICENSOR to apply for an exemption from taxation as a nonprofit entity before such taxes are paid.

3. LICENSEE shall pay to the LICENSOR a portion of SUBLICENSING REVENUE received from a SUBLICENSEE in regard to the LICENSED PATENT RIGHTS as follows:

- 25% for SUBLICENSES executed prior to the first dosing of a LICENSED PRODUCT in humans.
- 12% for SUBLICENSES executed after the first dosing of a LICENSED PRODUCT in humans and before the first dosing of a LICENSED PRODUCT in a Phase II human clinical trial. This percentage also applies to SUBLICENSES that are strictly for LICENSED PRODUCTS that are either a medical device or diagnostic, after such device or diagnostic is first used in a Phase I human clinical trial.
- 8% for SUBLICENSES executed after the first dosing of a LICENSED PRODUCT in a Phase II human clinical trial and before the first dosing of a LICENSED PRODUCT in a Phase III human clinical trial. This percentage also applies to SUBLICENSES that are strictly for LICENSED PRODUCTS that are either a medical device or diagnostic, after such device or diagnostic is first used in a Phase II human clinical trial.
- 5% for SUBLICENSES executed after the first dosing of a LICENSED PRODUCT in a Phase III human clinical trial and before the first filing of a New Drug Application ("NDA") or foreign equivalent for the first LICENSED PRODUCT. This percentage also applies to SUBLICENSES that are strictly for LICENSED PRODUCTS that are either a medical device or diagnostic, after such device or diagnostic is first used in a Phase III human clinical trial.
- 2% for SUBLICENSES executed after the first filing of a NDA or foreign equivalent for the first LICENSED PRODUCT (or in the case of a medical device or diagnostic being a LICENSED PRODUCT, the first filing of a Premarket Approval Application (PMA) or Premarket Notification (PMN) or 510(k) or foreign equivalent for the first LICENSED PRODUCT).

4. To maintain a license to the LICENSED PATENT RIGHTS, LICENSEE agrees to make Annual Minimum Payments in the amount of thirty thousand dollars ($30,000.00) that shall start on the first anniversary of the EFFECTIVE DATE and every anniversary thereafter as long as this Agreement is in effect. Such amounts shall be creditable on an annual basis against royalties on NET SALES of LICENSED PRODUCTS for that calendar year.

5. LICENSEE agrees to make the following one time only milestone payments to LICENSOR:

a. $150,000 due within thirty (30) days after the first filing of an Investigational New Drug Application (IND) with FDA or foreign equivalent for the first LICENSED PRODUCT in a MAJOR MARKET country by LICENSEE, a SUBLICENSEE or an AFFILIATE.

b. $1,000,000 due within thirty (30) days after the first commercial sale of the first LICENSED PRODUCT pursuant to an NDA (or foreign equivalent) approval, by LICENSEE, a SUBLICENSEE or an AFFILIATE.

c. $1,000,000 due within thirty (30) days after the achievement of $250,000,000 in aggregate worldwide NET SALES of LICENSED PRODUCTS by LICENSEE, its SUBLICENSEE(S) and its AFFILIATE(S).

d. $2,000,000 due within thirty (30) days after the achievement of $500,000,000 in aggregate worldwide NET SALES of LICENSED PRODUCTS by LICENSEE, its SUBLICENSEE(S) and its AFFILIATE(S).

LICENSEE shall timely notify LICENSOR of the achievement of each of the above milestones. Milestone payments shall be paid within thirty days after achievement of a milestone or receipt of an invoice whichever is later.

APPENDIX C
IIA

Confidential treatment has been sought for portions of this agreement. The copy filed herewithin omits the information subject to the confidential treatment request. Omissions are designated as *. A complete version of this exhibit has been filed separately with the Securities and Exchange Commission.**

Exhibit 10.4

AMENDMENT NO. 1 TO EXCLUSIVE LICENSE AGREEMENT

THIS AMENDMENT No. 1 TO EXCLUSIVE LICENSE AGREEMENT is entered into on July 2, 2015 (the "Effective Date of the Amendment"), by and between DURECT Corporation ("Company") and Virginia Commonwealth University Intellectual Property Foundation ("VCUIPF").

WHEREAS, Company and VCUIPF are parties to an Exclusive License Agreement dated December 5, 2012 (the "Agreement"), and

WHEREAS, the parties now wish to amend the Agreement as provided for herein.

NOW, THEREFORE, in consideration of the foregoing and the covenants and promises contained in this Amendment, the parties do hereby agree as follows:

1. Appendix A of the Agreement is hereby amended by deleting it in its entirety and replacing it with the Appendix A attached hereto and made a part hereof.

2. All capitalized terms not otherwise defined in this Amendment shall have the same meanings that are ascribed to them in the Agreement.

3. Except as expressly amended by this Amendment, the Agreement shall remain unchanged and continue in full force and effect as provided therein. This Amendment and the Agreement constitute the complete, final and exclusive understanding and agreement of the parties with respect to the subject matter of the Agreement, and supersede any and all prior or contemporaneous negotiations, correspondence, understandings and agreements, whether oral or written, between the parties respecting the subject matter of the Agreement. This Amendment may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the parties hereto have executed this Amendment in duplicate originals by their authorized officers as of the Effective Date of the Amendment.

DURECT CORPORATION	VIRGINIA COMMONWEALTH UNIVERSITY INTELLECTUAL PROPERTY FOUNDATION
By: /s/ Steve Helmer	By: /s/ Ivelina Metcheva
Name: Steve Helmer	Name: Ivelina Metcheva Phd, MBA

Confidential treatment has been sought for portions of this agreement. The copy filed herewithin omits the information subject to the confidential treatment request. Omissions are designated as *. A complete version of this exhibit has been filed separately with the Securities and Exchange Commission.**

Title:	VP, Chief Patent Counsel	Title:	President
Date:	July 2, 2015	Date:	July 1,2015

Confidential treatment has been sought for portions of this agreement. The copy filed herewithin omits the information subject to the confidential treatment request. Omissions are designated as *. A complete version of this exhibit has been filed separately with the Securities and Exchange Commission.**

APPENDIX A
LICENSED PATENT RIGHTS

U.S. Patent Applications:

Provisional Serial No. 60/621,537, filed October 25, 2004	Nuclear Oxysterol, Potent Regulator Of Cholesterol Homeostasis, For Therapy Of Hypercholesterolemia, Hyperlipidemia, and Atherosclerosis
Non-Provisional Serial No. 11/739,330, filed April 26, 2007	Nuclear Sulfated Oxysterol, Potent Regulator Of Cholesterol Homeostasis, For Therapy Of Hypercholesterolemia, Hyperlipidemia, and Atherosclerosis
Provisional Serial No. 61/154,063, filed February 20, 2009	5-Cholesten-3b , 25-diol 3-sulfate (25HC3S), an authentic PPARy agonist and LXR antagonist, or the therapy of inflammatory diseases
Non-Provisional Serial No. 12/708,803, filed February 19, 2010	Nuclear Sulfated Oxysterol, Potent Regulator Of Lipid Homeostasis, For Therapy Of Hypercholesterolemia, Hypertriglycerides, Fatty Liver Diseases, and Atherosclerosis
Provisional Serial No. 61/472,293, filed April 6, 2011	Hydroxysteroid sulfotransferase (SULT2B1b) for therapy of hyperlipidemia and fatty liver diseases
Non-Provisional Serial No. 13/441,241, filed April 6, 2012	Sulfated Oxysterol and Oxysterol Sulfation by Hydroxysterol Sulfotransferase Promote Lipid Homeostasis and Liver Proliferation
Provisional Serial No. 61/604,711, filed February 29, 2012	Sulfated oxysterol, 25HC3S and oxysterol sulfation by hydroxysterol sulfotransferase (SULT2Blb) promote liver proliferation: therapy for cirrhosis, injury, recovery following hepatectomy, and other applications
Provisional Serial No. 61/623,203, filed April 12, 2012 Provisional Serial No. 61/623,414, filed April 12, 2012	A Novel Cholesterol Metabolite, 5-Cholesten, 3-,25-diol, Disulfate (25HCDS) for Therapy of Metabolic Disorders, Hyperlipidemia, Fatty Liver Disease, Diabetes and Atherosclerosis
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VCU Invention Disclosures

VCU Invention Disclosure No.	Title
REN-04-072, disclosed September 24, 2004	Nuclear oxysterol, potent regulator of cholesterol hemeostasis, for therapy of hypercholesterolemia, hyperlipidemia, and atherosclerosis
REN-08-078, disclosed December 15, 2008	5-Cholesten-3b, 25-diol 3-sulfate (25HC3S), an authentic PPARy agonist and LXR antagonist, for the therapy of inflammatory diseases, such as inflammatory bowel diseases, fat liver diseases, and atheroclerotic diseases
REN-11-030, disclosed April 5, 2011	Hydroxysteroid sulfotransferase (SULT2B1b) for therapy of hyperlipidemia and fatty liver diseases

REN-11-93, disclosed November 7, 2011	Sulfated oxysterols, 25HC3S and 25HCDS, and oxysterol sulfation by hydroxysterol sulfotransferase (SULT2B1b) promote liver proliferation: therapy for cirrhosis, injury, and recovery following hepatectomy
REN-11-94, disclosed November 7, 2011	A novel cholesterol metabolite, 5-cholesten, 3-,25-diol, disulfate (25HCDS) for therapy of metabolic disorders, hyperlipidemia, diabetes, fat liver diseases, and atherosclerosis
REN-12-025, disclosed March 26, 2012	A Novel Cholesterol Metabolite, 5-Cholesten, 3-,25-diol, Disulfate (25HCDS) for Therapy of Metabolic Disorders, Hyperlipidemia, Diabetes, Fat Liver Diseases, and Atherosclerosis
REN-12-061, disclosed June 21, 2012	Novel Oxysterol, 5-Cholesten 3,27-diol 27-Glucuronide, for Therapy of Hypertriglyceridemia
REN-12-075	Low Levels of Oxysterol Sulfates, 25-,24, and 27(26)-hydroxycholesterol Sulfates, as biomarkers for diagnosis of lipid metabolic disorders, nonalcoholic fatty liver diseases
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Confidential treatment has been sought for portions of this agreement. The copy filed herewithin omits the information subject to the confidential treatment request. Omissions are designated as *. A complete version of this exhibit has been filed separately with the Securities and Exchange Commission.**

Exhibit 10.5

AMENDMENT NO. 2 TO EXCLUSIVE LICENSE AGREEMENT

THIS AMENDMENT No. 2 TO EXCLUSIVE LICENSE AGREEMENT is entered into on March 6, 2018 (the "Effective Date of the Amendment"), by and between DURECT Corporation ("Company") and Virginia Commonwealth University Intellectual Property Foundation ("VCUIPF").

WHEREAS, Company and VCUIPF are parties to an Exclusive License Agreement dated December 5, 2012, as amended (the "Agreement"), and

WHEREAS, the parties now wish to further amend the Agreement as provided for herein.

NOW, THEREFORE, in consideration of the foregoing and the covenants and promises contained in this Amendment, the parties do hereby agree as follows:

1. ***Appendix A of the Agreement is hereby amended by deleting it in its entirety and replacing it with the Appendix A attached hereto and made a part hereof.***

2. Section 1.10 of the Agreement is hereby amended by deleting it in its entirety and replacing it with the following:

   "IMPROVEMENT(S)" means [* * *].

3. Section 1.26 of the Agreement is hereby amended by deleting it in its entirety and replacing it with the following:

   "SRA" means the Sponsored Research Agreement by and between VCU and LICENSEE, effective May 7, 2012, as amended."

4. Sections 2.3(b), (c) and (d) of the Agreement are hereby amended by [* * *].

5. All capitalized terms not otherwise defined in this Amendment shall have the same meanings that are ascribed to them in the Agreement.

6. Except as expressly amended by this Amendment, the Agreement shall remain unchanged and continue in full force and effect as provided therein. This Amendment and the Agreement constitute the complete, final and exclusive understanding and agreement of the parties with respect to the subject matter of the Agreement, and supersede any and all prior or contemporaneous negotiations, correspondence, understandings and agreements, whether oral or written, between the parties respecting the subject matter of the Agreement. This Amendment may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

Confidential treatment has been sought for portions of this agreement. The copy filed herewithin omits the information subject to the confidential treatment request. Omissions are designated as *. A complete version of this exhibit has been filed separately with the Securities and Exchange Commission.**

IN WITNESS WHEREOF, the parties hereto have executed this Amendment in duplicate originals by their authorized officers as of the Effective Date of the Amendment.

DURECT CORPORATION	VIRGINIA COMMONWEALTH UNIVERSITY INTELLECTUAL PROPERTY FOUNDATION
By: /s/ James E. Brown	By: /s/ Ivelina Metcheva
Name: James E. Brown, D.V.M	Name: Ivelina Metcheva Phd, MBA
Title: CEO	Title: President
Date: March 6, 2018	Date: March 8, 2018

Confidential treatment has been sought for portions of this agreement. The copy filed herewithin omits the information subject to the confidential treatment request. Omissions are designated as *. A complete version of this exhibit has been filed separately with the Securities and Exchange Commission.**

APPENDIX A

LICENSED PATENT RIGHTS

Patents and Applications:

Nuclear Sulfated Oxysterol, Potent Regulator of Cholesterol Homeostasis, for Therapy of Hypercholesterolemia, Hyperlipidemia, and Atherosclerosis

	Sub Case	Case Type	Status	App. No.	Filing Date	Patent No.	Issue Date
		PRI	Inactive	60/621,537	25-Oct-2004		
	0	ORD	Published	11/739,330	24-Apr-2007		
	00	PRO	Inactive	61/154,063	20-Feb-2009		
	[* * *]	[* * *]	[* * *]	[* * *]	[* * *]	[* * *]	[* * *]
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	1	CIP	Granted	12/708,803	19-Feb-2010	8,399,441	19-Mar-2013
	[* * *]	[* * *]	[* * *]	[* * *]	[* * *]		

Sulfated Oxysterol and Oxysterol Sulfation by Hydroxysterol Sulfotransferase Promote Lipid Homeostasis and Liver Regeneration

	Sub Case	Case Type	Status	App. No.	Filing Date	Patent No.	Issue Date
		ORD	Granted	13/441,241	06-Apr-2012	9,034,859	19-May-2015
	0	PRO	Inactive	61/604,711	29-Feb-2012		
	00	PRO	Inactive	61/472,293	06-Apr-2011		
	[* * *]	[* * *]	[* * *]	[* * *]	[* * *]	[* * *]	[* * *]
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A Novel Cholesterol Metabolite, 5-cholesten, 3B- 25- diol, disulfate (25HCDS) for Therapy of Metabolic Disorders, Hylerlipidemia, Diabetes, Fatty Liver Diseases, and Atherosclerosis

	Sub Case	Case Type	Status	App. No.	Filing Date	Patent No.	Issue Date
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	01	PRO	Inactive	61/623,203	12-Apr-2012		
	02	PRO	Inactive	61/623,414	12-Apr-2012		
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VCU Invention Disclosures

VCU Invention Disclosure No.	**Title**
REN-04-072	Nuclear oxysterol, potent regulator of cholesterol hemeostasis, for therapy of hypercholesterolemia, hyperlipidemia, and atherosclerosis
REN-08-078F	5-Cholesten-3b, 25-diol 3-sulfate (25HC3S), an authentic PPARy agonist and LXR antagonist, for the therapy of inflammatory diseases, such as inflammatory bowel diseases, fat liver diseases, and atheroclerotic diseases
REN-11-030	Hydroxysteroid sulfotransferase (SULT2B1b) for therapy of hyperlipidemia and fatty liver diseases
REN-11-93	Sulfated oxysterols, 25HC3S and 25HCDS, and oxysterol sulfation by hydroxysterol sulfotransferase (SULT2B1b) promote liver proliferation: therapy for cirrhosis, injury, and recovery following hepatectomy

Confidential treatment has been sought for portions of this agreement. The copy filed herewithin omits the information subject to the confidential treatment request. Omissions are designated as *. A complete version of this exhibit has been filed separately with the Securities and Exchange Commission.**

REN-11-94	A novel cholesterol metabolite, 5-cholesten, 3-,25-diol, disulfate (25HCDS) for therapy of metabolic disorders, hyperlipidemia, diabetes, fat liver diseases, and atherosclerosis
REN-12-025	A Novel Cholesterol Metabolite, 5-Cholesten, 3-,25-diol, Disulfate (25HCDS) for Therapy of Metabolic Disorders, Hyperlipidemia, Diabetes, Fat Liver Diseases, and Atherosclerosis
REN-12-061	Novel Oxysterol, 5-Cholesten 3,27-diol 27-Glucuronide, for Therapy of Hypertriglyceridemia
REN-12-075	Low Levels of Oxysterol Sulfates, 25-,24, and 27(26)-hydroxycholesterol Sulfates, as biomarkers for diagnosis of lipid metabolic disorders, nonalcoholic fatty liver diseases
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Exhibit 31.1

Rule 13a-14(a) Section 302 Certification

CERTIFICATIONS

I, James E. Brown, certify that:

1. I have reviewed this quarterly report on Form 10-Q of DURECT Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent function):

   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

November 8, 2018

/S/ JAMES E. BROWN

James E. Brown
Chief Executive Officer

Exhibit 31.2

Rule 13a-14(a) Section 302 Certification

CERTIFICATIONS

I, Michael H. Arenberg, certify that:

1. I have reviewed this quarterly report on Form 10-Q of DURECT Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent function):

   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

November 8, 2018

/S/ MICHAEL H. ARENBERG

Michael H. Arenberg
Chief Financial Officer and
Principal Accounting Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of DURECT Corporation (the "Company") on Form 10-Q for the period ending September 30, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, James E. Brown, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

November 8, 2018

/S/ JAMES E. BROWN

James E. Brown
Chief Executive Officer

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of DURECT Corporation (the "Company") on Form 10-Q for the period ending September 30, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Michael H. Arenberg, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

November 8, 2018

/S/ MICHAEL H. ARENBERG

Michael H. Arenberg
Chief Financial Officer and
Principal Accounting Officer