

REGULUS THERAPEUTICS INC.

FORM 10-Q (Quarterly Report)

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**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2016

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: 001-35670

Regulus Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

26-4738379
(I.R.S. Employer
Identification No.)

10614 Science Center Drive
San Diego, CA
(Address of Principal Executive Offices)

92121
(Zip Code)

858-202-6300
(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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes No

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company	<input type="checkbox"/>

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

As of July 29, 2016, the registrant had 52,820,326 shares of Common Stock (\$0.001 par value) outstanding.

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PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

Regulus Therapeutics Inc.
CONDENSED BALANCE SHEETS
(in thousands, except share and per share data)

	June 30, 2016	December 31, 2015
	(Unaudited)	
Assets		
Current assets:		
Cash and cash equivalents	\$ 27,040	\$ 15,960
Short-term investments	80,502	98,103
Restricted cash	462	1,256
Prepaid expenses	7,565	8,159
Contract and other receivables	143	10,021
Other current assets	522	759
Total current assets	116,234	134,258
Property and equipment, net	12,322	5,400
Intangibles, net	1,062	1,081
Other assets	310	344
Total assets	\$ 129,928	\$ 141,083
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 3,504	\$ 2,717
Accrued liabilities	5,472	6,329
Accrued compensation	1,863	2,392
Current portion of deferred revenue	258	1,194
Total current liabilities	11,097	12,632
Term loan, less debt issuance costs	19,786	—
Deferred revenue, less current portion	2,029	2,065
Other long-term liabilities	8,570	2,308
Total liabilities	41,482	17,005
Commitments and Contingencies		
Stockholders' equity:		
Common stock, \$0.001 par value; 200,000,000 shares authorized, 52,787,756 and 52,669,266 shares issued and outstanding at June 30, 2016 (unaudited) and December 31, 2015, respectively	53	53
Additional paid-in capital	322,287	315,673
Accumulated other comprehensive loss	(83)	(133)
Accumulated deficit	(233,811)	(191,515)
Total stockholders' equity	88,446	124,078
Total liabilities and stockholders' equity	\$ 129,928	\$ 141,083

See accompanying notes to these condensed financial statements.

Regulus Therapeutics Inc.
CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Three months ended June 30,		Six months ended June 30,	
	2016	2015	2016	2015
(Unaudited)				
Revenues:				
Revenue under strategic alliances and collaborations	\$ 483	\$ 3,834	\$ 972	\$ 8,034
Total revenues	483	3,834	972	8,034
Operating expenses:				
Research and development	18,007	19,201	34,772	32,628
General and administrative	3,664	5,814	8,767	9,458
Total operating expenses	21,671	25,015	43,539	42,086
Loss from operations	(21,188)	(21,181)	(42,567)	(34,052)
Other income (expense):				
Interest and other income	180	151	372	351
Interest and other expense	(90)	(7)	(114)	(16)
Loss from valuation of convertible note payable	—	—	—	(1,811)
Loss before income taxes	(21,098)	(21,037)	(42,309)	(35,528)
Income tax benefit	8	2	13	6
Net loss	\$ (21,090)	\$ (21,035)	\$ (42,296)	\$ (35,522)
Other comprehensive loss:				
Unrealized gain (loss) on short-term investments, net	9	(2)	50	55
Comprehensive loss	\$ (21,081)	\$ (21,037)	\$ (42,246)	\$ (35,467)
Net loss per share, basic and diluted	\$ (0.40)	\$ (0.41)	\$ (0.80)	\$ (0.70)
Weighted average shares used to compute basic and diluted net loss per share	52,782,643	51,073,488	52,746,657	50,575,096

See accompanying notes to these condensed financial statements.

Regulus Therapeutics Inc.
CONDENSED STATEMENTS OF CASH FLOWS
(In thousands)

	Six months ended June 30,	
	2016	2015
	(Unaudited)	
Operating activities		
Net loss	\$ (42,296)	\$ (35,522)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	928	798
Loss from valuation of convertible note payable	—	1,811
Stock-based compensation	5,986	8,972
Amortization of premium on investments, net	359	801
Other	45	56
Change in operating assets and liabilities:		
Contracts and other receivables	9,878	(50)
Prepaid expenses	594	826
Other assets	270	20
Accounts payable	787	130
Accrued liabilities	(1,063)	2,459
Accrued compensation	(529)	167
Deferred revenue	(972)	(1,323)
Deferred rent and other liabilities	(262)	(160)
Net cash used in operating activities	<u>(26,275)</u>	<u>(21,015)</u>
Investing activities		
Purchases of short-term investments	(30,231)	(46,281)
Sales and maturities of short-term investments	47,522	49,645
Purchases of property and equipment	(266)	(410)
Acquisition of intangibles	(34)	(19)
Net cash provided by investing activities	<u>16,991</u>	<u>2,935</u>
Financing activities		
Proceeds from borrowing under term loan, net	19,819	—
Proceeds from issuance of common stock, net	363	257
Proceeds from exercise of common stock options	265	1,655
Principal payments on other long-term obligations	(83)	(75)
Net cash provided by financing activities	<u>20,364</u>	<u>1,837</u>
Net increase (decrease) in cash and cash equivalents	11,080	(16,243)
Cash and cash equivalents at beginning of period	15,960	37,327
Cash and cash equivalents at end of period	<u>\$ 27,040</u>	<u>\$ 21,084</u>
Supplemental disclosure of cash flow information		
Net changes in restricted cash	<u>\$ (794)</u>	<u>\$ —</u>
Interest paid	<u>\$ (54)</u>	<u>\$ (15)</u>
Income taxes paid	<u>\$ (1)</u>	<u>\$ (1)</u>
Supplemental disclosure of non-cash investing and financing activities		
Allowance for tenant improvements	<u>\$ 6,545</u>	<u>\$ —</u>
Amounts accrued for property and equipment	<u>\$ 221</u>	<u>\$ 90</u>
Amounts accrued for patent expenditures	<u>\$ 7</u>	<u>\$ —</u>
Unpaid debt issuance costs	<u>\$ 38</u>	<u>\$ —</u>

See accompanying notes to these condensed financial statements.

Regulus Therapeutics Inc.
NOTES TO CONDENSED FINANCIAL STATEMENTS
(Unaudited)

1. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed financial statements have been prepared in accordance with U.S. generally accepted accounting principles (“GAAP”) for interim financial information and the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. In management’s opinion, the accompanying financial statements reflect all adjustments, consisting of normal recurring adjustments, considered necessary for a fair presentation of the results for the interim periods presented.

Interim financial results are not necessarily indicative of results anticipated for the full year. These unaudited condensed financial statements should be read in conjunction with the audited financial statements and footnotes included in our Annual Report on Form 10-K for the year ended December 31, 2015, from which the balance sheet information herein was derived.

Use of Estimates

Our condensed financial statements are prepared in accordance with GAAP, which requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements and accompanying notes. An estimated loss contingency is accrued in our financial statements if it is probable that a liability has been incurred and the amount of the loss can be reasonably estimated. Although these estimates are based on our knowledge of current events and actions we may undertake in the future, actual results may ultimately differ from these estimates and assumptions.

Revenue Recognition

Our revenues generally consist of upfront payments for licenses or options to obtain licenses in the future, milestone payments and payments for other research services under strategic alliance and collaboration agreements. We recognize revenues when all four of the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery of the products and/or services has occurred; (3) the selling price is fixed or determinable; and (4) collectability is reasonably assured.

Multiple element arrangements, such as our strategic alliance agreements with Sanofi and AstraZeneca AB (“AstraZeneca”), are analyzed to determine whether the deliverables within the agreement can be separated or whether they must be accounted for as a single unit of accounting. Deliverables under the agreement will be accounted for as separate units of accounting provided that (i) a delivered item has value to the customer on a stand-alone basis; and (ii) if the agreement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the control of the vendor. The allocation of consideration amongst the deliverables under the agreement is derived using a “best estimate of selling price” if vendor specific objective evidence and third-party evidence of fair value is not available. If the delivered element does not have stand-alone value, the arrangement is then accounted for as a single unit of accounting, and we recognize the consideration received under the arrangement as revenue on a straight-line basis, which approximates effort over our estimated period of performance, which for us is often the expected term of the research and development plan.

Milestones

We apply the milestone method of accounting to recognize revenue from milestone payments when earned, as evidenced by written acknowledgment from the collaborator or other persuasive evidence that the milestone has been achieved and the payment is non-refundable, provided that the milestone event is substantive. A milestone event is defined as an event (i) that can only be achieved based in whole or in part on either our performance or on the occurrence of a specific outcome resulting from our performance; (ii) for which there is substantive uncertainty at the inception of the arrangement that the event will be achieved; and (iii) that would result in additional payments being due to us. Events for which the occurrence is either contingent solely upon the passage of time or the result of a counterparty’s performance are not considered to be milestone events. A milestone event is substantive if all of the following conditions are met: (i) the consideration is commensurate with either our performance to achieve the milestone, or the enhancement of the value to the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone; (ii) the consideration relates solely to past performance; and (iii) the consideration is reasonable relative to all the deliverables and payment terms (including other potential milestone consideration) within the arrangement.

We assess whether a milestone is substantive at the inception of each arrangement. If a milestone is deemed non-substantive, we will account for that milestone payment using a method consistent with the related units of accounting for the arrangement over the related performance period.

Deferred Revenue

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying balance sheets. Amounts not expected to be recognized within the next 12 months are classified as non-current deferred revenue.

Stock-Based Compensation

We account for stock-based compensation expense related to stock options granted to employees and members of our board of directors by estimating the fair value of each stock option on the date of grant using the Black-Scholes option pricing model. We recognize stock-based compensation expense using the accelerated multiple-option approach. Under the accelerated multiple-option approach (also known as the graded-vesting method), we recognize compensation expense over the requisite service period for each separately vesting tranche of the award as though the award was in substance multiple awards, resulting in accelerated expense recognition over the vesting period. For performance-based awards granted to employees (i) the fair value of the award is determined on the grant date, (ii) we assess the probability of the individual milestones under the award being achieved and (iii) the fair value of the shares subject to the milestone is expensed over the implicit service period commencing once management believes the performance criteria is probable of being met.

We account for stock options granted to non-employees using the fair value approach. Stock options granted to non-employees are subject to periodic revaluation over their vesting terms.

Fair Value Option

Applicable accounting policies permit entities to choose, at specified election dates, to measure specified items at fair value if the decision about the election is: (1) applied instrument by instrument, (2) irrevocable, and (3) applied to an entire instrument. The balance of our convertible note payable, which was valued under the fair value option, was converted into shares of common stock in January 2015 (see Note 4).

Clinical Trial and Preclinical Study Accruals

We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on the facts and circumstances known to us at that time. Our accrued expenses for preclinical studies and clinical trials are based on estimates of costs incurred and fees that may be associated with services provided by clinical trial investigational sites, clinical research organizations (“CROs”) and for other clinical trial-related activities. Payments under certain contracts with such parties depend on factors such as successful enrollment of patients, site initiation and the completion of clinical trial milestones. In accruing for these services, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If possible, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate these services based on other information available to us. If we underestimate or overestimate the activities or fees associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, our estimated accrued liabilities have approximated actual expense incurred. Subsequent changes in estimates may result in a material change in our accruals.

Restricted Cash

Restricted cash consists of amounts received for a specific and limited purpose, and therefore not available for general operating activities. In August 2015, we received \$1.4 million in connection with our facility lease agreement with Walton Torrey Owner B, L.L.C, entered into in July 2015. The use of these funds are restricted to costs associated with the relocation of our corporate headquarters. As of June 30, 2016, our restricted cash balance was \$0.5 million.

Prepaid Expenses

We capitalize the purchase of certain raw materials and related supplies for use in the manufacturing of drug product in our clinical development programs, as we have determined that these materials have alternative future use. We can use these raw materials and related supplies in multiple clinical drug products, and therefore have future use independent of the development status of any particular drug program until it is utilized in the manufacturing process. We periodically review these capitalized materials for indicators of impairment, including shelf life, continued alternative future use and obsolescence.

We have not recorded any adjustments to the carrying value of these materials to date. These materials are recorded as prepaid expenses in our consolidated balance sheets.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-09, *Revenue from Contracts with Customers*. Adoption of ASU No. 2014-09 requires that an entity recognize revenue to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. This update is effective for annual reporting periods beginning after December 15, 2017 and interim periods therein and requires expanded disclosures. We are currently evaluating the impact of adoption on our financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements Going Concern*, which requires management to assess an entity's ability to continue as a going concern, and to provide related footnote disclosure in certain circumstances. This standard is effective for annual reporting periods ending after December 15, 2016 and interim periods thereafter. Early application is permitted. The adoption of this guidance will have no impact on our financial statements.

In April 2015, the FASB issued ASU No. 2015-03, *Interest- Imputation of Interest: Simplifying the Presentation of Debt Issuance Costs*, which requires that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. The recognition and measurement guidance for debt issuance costs were not affected by the amendments in ASU No. 2015-03. In June 2016, upon entering into a loan and security agreement, we adopted ASU No. 2015-03, which resulted in the classification of \$0.2 million of debt issuance costs against the principal balance of our outstanding Term Loan of \$20.0 million.

In January 2016, the FASB issued ASU No. 2016-01, *Recognition and Measurement of Financial Assets and Financial Liabilities*, which eliminates the requirement for public companies to disclose the method(s) and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost on the balance sheet. Additionally, the standard requires public entities to use the exit price notion when measuring the fair value of financial instruments for disclosure purposes. Furthermore, the standard requires presentation of financial assets and liabilities by measurement category and form of financial asset on the balance sheet or accompanying notes to the financial statements. The standard is effective for annual reporting periods beginning after December 15, 2017, including interim periods within those annual reporting periods. Early application is permitted. We are currently evaluating the impact of adoption on our financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases*, which increases transparency and comparability among organizations by requiring recognition of lease assets and lease liabilities on the balance sheet and disclosure of key information about leasing arrangements. The standard is effective for annual reporting periods beginning after December 15, 2018, including interim periods within those annual reporting periods. Early application is permitted. We are currently evaluating the impact of adoption on our financial statements.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation – Stock Compensation: Improvements to Employee Share-Based Payment Accounting*, which is intended to simplify several aspects of accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. The standard is effective for annual reporting periods beginning after December 15, 2016, and interim periods within those annual reporting periods. Early application is permitted. We are currently evaluating the impact of adoption on our financial statements.

2. Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by dividing net loss by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. Dilutive common stock equivalents are comprised of options outstanding under our stock option plans. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted net loss per share.

Potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive consisted of 3,055,143 and 2,639,630 shares attributable to common stock options for the three and six months ended

June 30, 2016 , respectively, compared to 2,905,340 and 3,331,699 shares attributable to common stock options for the same periods in 2015 .

3. Investments

We invest our excess cash in commercial paper and debt instruments of financial institutions and corporations. As of June 30, 2016 , our short-term investments had a weighted average maturity of less than two years.

The following tables summarize our short-term investments (in thousands):

	Maturity (in years)	Amortized cost	Unrealized		Estimated fair value
			Gains	Losses	
As of June 30, 2016					
Corporate debt securities	2 or less	\$ 65,725	\$ 8	\$ (26)	\$ 65,707
Certificates of deposit	2 or less	9,800	—	—	9,800
Commercial paper	1 or less	4,983	12	—	4,995
Total		\$ 80,508	\$ 20	\$ (26)	\$ 80,502

	Maturity (in years)	Amortized cost	Unrealized		Estimated fair value
			Gains	Losses	
As of December 31, 2015					
Corporate debt securities	2 or less	\$ 81,054	\$ 16	\$ (103)	\$ 80,967
Certificates of deposit	2 or less	13,640	—	—	13,640
Commercial paper	1 or less	3,490	6	—	3,496
Total		\$ 98,184	\$ 22	\$ (103)	\$ 98,103

4. Fair Value Measurements

We have certain financial assets recorded at fair value which have been classified as Level 1, 2, or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements.

Accounting standards define fair value 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 as of the measurement date. Market participants are buyers and sellers in the principal market that are (i) independent, (ii) knowledgeable, (iii) able to transact, and (iv) willing to transact. The accounting standards provide an established hierarchy for inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the most observable inputs be used when available. Observable inputs are inputs that market participants would use in valuing the asset or liability and are developed based on market data obtained from independent sources. Unobservable inputs are inputs that reflect our assumptions about the factors that market participants would use in valuing the asset or liability. The accounting standards prioritize the inputs used in measuring the fair value into the following hierarchy:

- Level 1 includes financial instruments for which quoted market prices for identical instruments are available in active markets.
- Level 2 includes financial instruments for which there are inputs other than quoted prices included within Level 1 that are observable for the instrument such as quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets with insufficient volume or infrequent transactions (less active markets) or model-driven valuations in which significant inputs are observable or can be derived principally from, or corroborated by, observable market data.
- Level 3 includes financial instruments for which fair value is derived from valuation techniques in which one or more significant inputs are unobservable, including management's own assumptions.

Financial Assets Measured at Fair Value

The following table presents our fair value hierarchy for assets measured at fair value on a recurring basis as of June 30, 2016 and December 31, 2015 (in thousands):

	Fair value as of June 30, 2016			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	\$ 17,443	\$ 17,443	\$ —	\$ —
Corporate debt securities	65,707	—	65,707	—
Certificates of deposit	9,800	—	9,800	—
Commercial paper	4,995	—	4,995	—
	<u>\$ 97,945</u>	<u>\$ 17,443</u>	<u>\$ 80,502</u>	<u>\$ —</u>

	Fair value as of December 31, 2015			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	\$ 15,152	\$ 15,152	\$ —	\$ —
Corporate debt securities	80,967	—	80,967	—
Certificates of deposit	13,640	—	13,640	—
Commercial paper	3,496	—	3,496	—
	<u>\$ 113,255</u>	<u>\$ 15,152</u>	<u>\$ 98,103</u>	<u>\$ —</u>

We obtain pricing information from quoted market prices or quotes from brokers/dealers. We generally determine the fair value of our investment securities using standard observable inputs, including reported trades, broker/dealer quotes, bids and/or offers. Refer to Note 3 for information regarding our investments.

Financial Liabilities Measured at Fair Value

In October 2012, in conjunction with our initial public offering, an amended and restated convertible promissory note originally issued to Glaxo Group Limited in February 2010 rolled over into a new promissory note (the "Post-IPO GSK Note"). The Post-IPO GSK Note was established in the principal amount of \$5.4 million, with a maturity date of October 9, 2015. We used an income approach in the form of a convertible bond valuation model to value our convertible note payable. The convertible bond model considered the debt and option characteristics of the note.

On January 29, 2015, the principal amount outstanding under the Post-IPO GSK Note of \$5.4 million was converted into 1,356,738 shares of our common stock at a conversion price of \$4.00 per share. A final valuation upon conversion was performed, considering only the option characteristics of the note as its conversion was certain. Key inputs of volatility, risk-free rate and credit spread were considered, however, the final valuation was substantially driven by the number of shares of common stock issued upon conversion (1,356,738) and our stock price on the date of conversion (\$18.58). Upon issuance of the common stock, the fair value of the convertible note was classified into stockholders' equity. We recorded a loss from the change in valuation of the convertible note payable of \$1.8 million in the condensed statements of operations and comprehensive loss upon conversion in January 2015.

5. Term Loan

On June 17, 2016, we entered into a loan and security agreement ("Loan Agreement") with Oxford Finance, LLC, ("Oxford"), pursuant to which Oxford agreed to lend us up to \$30.0 million, issuable in two separate term loans of \$20.0 million (the "Term A Loan") and \$10.0 million (the "Term B Loan"). We collectively refer to the Term A Loan and the Term B Loan as Term Loans. On June 22, 2016, we received \$20.0 million in proceeds from the Term A Loan, net of debt issuance costs. Under the terms of the Loan Agreement we may, at our sole discretion, borrow \$10.0 million under the Term B Loan following the achievement of a defined milestone event until the earlier of 60 days thereafter or March 31, 2017.

All outstanding Term Loans will mature on June 1, 2020 (the "Maturity Date") and we will have interest-only payments through June 30, 2018, followed by 24 months of principal and interest payments. The Term Loans will bear interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S Dollar LIBOR rate reported in *The Wall*

Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44% .

We have the option to prepay all, but not less than all, of the borrowed amounts, provided that we will be obligated to pay a prepayment fee equal to (i) 2% of the outstanding principal balance of the applicable Term Loan if prepayment is made prior to the second anniversary of the applicable funding date of the Term Loan, provided no prepayment fee will be due in connection with a prepayment made on or prior to the first anniversary of the applicable funding date of the Term Loan in connection with an acquisition of our company, or (ii) 1% of the applicable Term Loan prepaid thereafter and prior to the Maturity Date. We will be required to make a final payment of 5.5% of the principal balance outstanding, payable on the earlier of (i) the Maturity Date, (ii) acceleration of any Term Loan, or (iii) the prepayment of the Term Loans.

We may use the proceeds from the Term Loans solely for working capital and to fund our general business requirements. Our obligations under the Loan Agreement are secured by a first priority security interest in substantially all of our current and future assets, other than our intellectual property. We have also agreed not to encumber our intellectual property assets, except as permitted by the Loan Agreement.

As of June 30, 2016, we had \$20.0 million outstanding under the Term A Loan. The Term A Loan was recorded at its initial carrying value of \$20.0 million , less debt issuance costs of approximately \$0.2 million . In connection with the Term A Loan, the debt issuance costs have been recorded as a debt discount in our consolidated balance sheets, which are being recorded as interest expense over the life of the Term A Loan using an effective interest rate of 8.98% . The exit fee is accrued over life of the Term A Loan through interest expense.

As of June 30, 2016, we were in compliance with all material covenants under the Loan Agreement.

Future principal payments for the Term A Loan due under the Loan Agreement are as follows (in thousands):

2016	\$	—
2017		—
2018		5,000
2019		10,000
2020		5,000
	\$	<u>20,000</u>

6. Stockholders' Equity

Shares Reserved for Future Issuance

The following shares of common stock were reserved for future issuance as of June 30, 2016 :

Common stock options outstanding	6,937,798
Common stock available for future grant under 2012 Equity Incentive Plan	2,164,263
Common stock available for future grant under 2015 Inducement Plan	581,806
Employee Stock Purchase Plan	1,697,431
Total common shares reserved for future issuance	<u>11,381,298</u>

The following table summarizes our stock option activity under all equity incentive plans for the six months ended June 30, 2016 (shares in thousands):

	Number of options	Weighted average exercise price
Options outstanding at December 31, 2015	5,126	\$ 8.91
Granted	2,375	\$ 6.62
Exercised	(56)	\$ 4.76
Canceled/forfeited/expired	(507)	\$ 10.47
Options outstanding at June 30, 2016	6,938	\$ 8.04

Stock-Based Compensation

The following table summarizes the weighted average assumptions used to estimate the fair value of stock options and performance stock awards granted to employees under our 2012 Equity Incentive Plan and 2015 Inducement Plan and the shares purchasable under our Employee Stock Purchase Plan during the periods presented:

	Three months ended June 30,		Six months ended June 30,	
	2016	2015	2016	2015
Stock options				
Risk-free interest rate	1.5%	1.8%	1.4%	1.8%
Volatility	79.1%	79.1%	79.7%	78.8%
Dividend yield	—	—	—	—
Expected term (years)	5.8	6.1	5.9	6.1
Performance stock options				
Risk-free interest rate	0.4%	—	1.4%	1.8%
Volatility	78.5%	—	79.3%	76.4%
Dividend yield	—	—	—	—
Expected term (years)	5.5	0	6.0	6.0
Employee stock purchase plan shares				
Risk-free interest rate	0.5%	0.1%	0.4%	0.1%
Volatility	82.6%	76.9%	81.0%	74.9%
Dividend yield	—	—	—	—
Expected term (years)	0.5	0.5	0.5	0.5

The following table summarizes the allocation of our stock-based compensation expense for all stock awards during the periods presented (in thousands):

	Three months ended June 30,		Six months ended June 30,	
	2016	2015	2016	2015
Research and development	\$ 1,299	\$ 3,496	\$ 2,731	\$ 5,452
General and administrative	939	2,373	3,255	3,520
Total	\$ 2,238	\$ 5,869	\$ 5,986	\$ 8,972

7. Strategic Alliances and Collaborations

The following table summarizes our total revenues from our strategic alliances and collaborations during the periods presented (in thousands):

	Three months ended June 30,		Six months ended June 30,	
	2016	2015	2016	2015
AstraZeneca	\$ 465	\$ 3,066	\$ 936	\$ 6,648
Sanofi	18	18	36	36
Biogen	—	750	—	1,350
Total	\$ 483	\$ 3,834	\$ 972	\$ 8,034

AstraZeneca

In August 2012, we entered into a collaboration and license agreement with AstraZeneca. Under the terms of the agreement, we have agreed to collaborate with AstraZeneca to identify, research and develop compounds targeting three *micro* RNA alliance targets primarily in the fields of cardiovascular diseases, metabolic diseases and oncology. Pursuant to the agreement, we granted AstraZeneca an exclusive, worldwide license to thereafter develop, manufacture and commercialize lead compounds designated by AstraZeneca in the course of the collaboration activities against the alliance targets for all human therapeutic uses. Under the terms of the agreement we are required to use commercially reasonable efforts to perform all research, development and manufacturing activities described in the research plan, at our cost, until the acceptance of an investigational new drug application ("IND") or the end of the research term, which extends until the fourth anniversary of the date of the agreement, or August 14, 2016, and may be extended only by mutual written agreement of us and AstraZeneca. Following the earlier to occur of the acceptance of an IND in a major market or the end of the research term, AstraZeneca will assume all costs, responsibilities and obligations for further development, manufacture and commercialization of alliance product candidates.

Under the terms of the agreement, we received an upfront payment of \$3.0 million in October 2012. We determined the elements within the agreement should be treated as a single unit of accounting because the delivered element, the license, does not have stand-alone value. As a result, we are recognizing revenue related to the upfront payment on a straight-line basis over our estimated period of performance, which is four years based on the expected term of the research and development plan, ending in August 2016.

Concurrently with the collaboration and license agreement, we entered into a Common Stock Purchase Agreement ("CSPA") with AstraZeneca, pursuant to which we agreed to sell to AstraZeneca an aggregate of \$25.0 million of our common stock in a private placement concurrently with our initial public offering, at a price per share equal to the initial public offering price. In October 2012, in accordance with the CSPA, we sold AstraZeneca 6,250,000 shares of our common stock at a price per share of \$4.00. Further, the CSPA stipulated that AstraZeneca could not sell, transfer, make any short sale of, or grant any option for the sale of any common stock for a 365-day period following the effective date of our initial public offering. Accounting standards for multiple element arrangements contains a presumption that separate contracts negotiated and/or entered into at or near the same time with the same entity were negotiated as a package and should be evaluated as a single agreement. We valued the discount applied to the shares of common stock due to the one-year restriction. Based upon restricted stock studies of similar duration and a Black-Scholes valuation to measure a discount for lack of marketability, \$4.3 million was attributed to the collaboration and license agreement. We continue to recognize the \$4.3 million into revenue ratably over the estimated period of performance of the collaboration. As of June 30, 2016, deferred revenue associated with the collaboration and license agreement and CSPA was \$0.2 million, which we are expecting to recognize over the remaining contractual term and corresponding estimated period of performance of approximately two months.

In March 2015, we earned a \$2.5 million preclinical milestone payment upon AstraZeneca's selection of RG-125, a GalNAc-conjugated anti-miR targeting *micro* RNA-103/107, as a lead compound under the agreement. In December 2015, we earned a \$10.0 million clinical milestone payment upon AstraZeneca's first patient dosing in a first-in-human Phase I clinical study of RG-125. If all three targets are successfully developed and commercialized through pre-agreed sales targets, we could receive additional milestone payments of up to \$485.5 million, including preclinical milestones of up to \$2.5 million upon selection of a lead compound, up to \$113.0 million for clinical milestones, and up to \$370.0 million for commercialization milestones. Specifically for RG-125, we could receive additional milestone payments of up to \$160.0 million, including up to \$32.5 million for clinical milestones and up to \$127.5 million for commercial milestones. In addition, we are entitled to receive royalties based on a percentage of net sales which will range from the mid-single digits to the low end of the 10 to 20% range, depending upon the product and the volume of sales, which royalties may be reduced in certain, limited circumstances.

We have evaluated the contingent event-based payments under our collaboration and license agreement with AstraZeneca and determined that the preclinical milestone and the milestone earned for the initiation of a Phase I clinical trial meet the definition of substantive milestones. Accordingly, revenue for these achievements was recognized in its entirety in the period when the milestone was achieved and collectability was reasonably assured. Other contingent event-based payments under the

agreement for which payment is contingent upon the results of AstraZeneca's performance will not be accounted for using the milestone method. Such payments will be recognized as revenue over the remaining estimated period of performance, if any, and when collectability is reasonably assured.

In January 2015, we entered into a letter agreement with AstraZeneca to amend the collaboration and license agreement. Under the terms of the letter agreement, we agreed to perform additional miR-103/107 program research and development activities related to RG-125. AstraZeneca agreed to fund 50% of the costs for these additional activities, as outlined in the letter agreement. In accordance with the collaboration and license agreement, AstraZeneca funded 100% of the costs for product manufacturing activities outlined in the letter agreement necessary to support a Phase I clinical study. In December 2015, we completed a technology transfer to AstraZeneca and have no further obligations to AstraZeneca for future development of RG-125. We recognized \$0.6 million and \$3.2 million for the three and six months ended June 30, 2015, respectively, for the performance of research and development and product manufacturing activities outlined in the letter agreement. As of December 31, 2015, our obligations under the letter agreement were complete.

Sanofi

In July 2012, we amended and restated our collaboration and license agreement with Sanofi to expand the potential therapeutic applications of the *micro* RNA alliance targets to be developed under such agreement. We determined that the elements within the strategic alliance agreement with Sanofi should be treated as a single unit of accounting because the delivered elements did not have stand-alone value to Sanofi. The following elements were delivered as part of the strategic alliance with Sanofi: (1) a license for up to four *micro* RNA targets; and (2) a research license under our technology alliance.

In June 2013, the original research term expired, upon which we and Sanofi entered into an option agreement pursuant to which Sanofi was granted an exclusive right to negotiate the co-development and commercialization of certain of our unencumbered *micro* RNA programs and we were granted the exclusive right to negotiate with Sanofi for co-development and commercialization of certain miR-21 anti-miRs in oncology and Alport syndrome. In July 2013, we received an upfront payment of \$2.5 million, of which \$1.25 million is creditable against future amounts payable by Sanofi to us under any future co-development and commercialization agreement we enter pursuant to the option agreement. Revenue associated with the creditable portion of this option payment remained deferred as of June 30, 2016, and will remain deferred until its application to a creditable transaction. The non-creditable portion of this payment, \$1.25 million, was recognized as revenue over the option period from the effective date of the option agreement in June 2013 through the expiration of the option period in January 2014.

In February 2014, we and Sanofi entered into a second amended and restated collaboration and license agreement (the "2014 Sanofi Amendment") to renew our strategic alliance to discover, develop and commercialize *micro* RNA therapeutics to focus on specific orphan disease and oncology targets. Under the terms of our renewed alliance, Sanofi will have opt-in rights to our preclinical fibrosis program targeting miR-21 for the treatment of Alport syndrome, our preclinical program targeting miR-21 for oncology indications, and our preclinical program targeting miR-221/222 for hepatocellular carcinoma ("HCC"). We are responsible for developing each of these programs to proof-of-concept, at which time Sanofi has an exclusive option on each program. If Sanofi chooses to exercise its option on any of these programs, Sanofi will reimburse us for a significant portion of our preclinical and clinical development costs and will also pay us an option exercise fee for any such program, provided that \$1.25 million of the \$2.5 million upfront option fee paid to us by Sanofi in connection with the June 2013 option agreement will be creditable against such option exercise fee. We are eligible to receive royalties on *micro* RNA therapeutic products commercialized by Sanofi and will have the right to co-promote these products.

In connection with the 2014 Sanofi Amendment, we entered into a Common Stock Purchase Agreement (the "Purchase Agreement"), pursuant to which we sold 1,303,780 shares of our common stock to Aventisub LLC (formerly Aventis Holdings, Inc.) ("Aventis"), an entity affiliated with Sanofi, in a private placement at a price per share of \$7.67 for an aggregate purchase price of \$10.0 million. Under the terms of the Purchase Agreement, Aventis was not permitted to sell, transfer, make any short sale of, or grant any option for the sale of any common stock for the 12-month period following its effective date. The Purchase Agreement and the 2014 Sanofi Amendment were negotiated concurrently and were therefore evaluated as a single agreement. Based upon restricted stock studies of similar duration and a Black-Scholes valuation to measure the discount for lack of marketability, approximately \$0.4 million of the proceeds from the Purchase Agreement was attributed to the 2014 Sanofi Amendment, and represents consideration for the value of the program targeting miR-221/222 for HCC. As this element does not have stand-alone value, we are recognizing the \$0.4 million allocated consideration into revenue ratably over the estimated period of performance of the miR-221/222 program. As of June 30, 2016, deferred revenue associated with the Purchase Agreement and the 2014 Sanofi Amendment was \$0.3 million, which we are expecting to recognize over the remaining estimated period of performance of approximately four years.

We are eligible to receive milestone payments of up to \$101.8 million for proof-of-concept option exercise fees (net of \$1.25 million creditable, as noted above), \$15.0 million for clinical milestones and up to \$300.0 million for regulatory and commercial milestones. In addition, we are entitled to receive royalties based on a percentage of net sales of any products from the miR-21 and miR-221/222 programs which, in the case of sales in the United States, will be in the middle of the 10 to 20% range, and, in the case of sales outside of the United States, will range from the low end to the middle of the 10 to 20% range, depending upon the volume of sales. If we exercise our option to co-promote a product, we will continue to be eligible to receive royalties on net sales of each product in the United States at the same rate, unless we elect to share a portion of Sanofi's profits from sales of such product in the United States in lieu of royalties.

We have evaluated the contingent event-based payments under the 2014 Sanofi Amendment and determined that the milestone payments meet the definition of substantive milestones. Accordingly, revenue for these achievements will be recognized in their entirety in the period when the milestone is achieved and collectability is reasonably assured. Other contingent event-based payments under the 2014 Sanofi Amendment for which payment is contingent upon the results of Sanofi's performance will not be accounted for using the milestone method. Such payments will be recognized as revenue over the remaining estimated period of performance, if any, and when collectability is reasonably assured.

Biogen

In August 2014, we entered into a collaboration and license agreement with Biogen to collaborate on *micro* RNA biomarkers for multiple sclerosis. Pursuant to the terms of the collaboration and license agreement, we received an upfront payment of \$2.0 million. We determined that the elements within the collaboration and license agreement were to be treated as a single unit of accounting because the delivered element, the license, did not have stand-alone value to Biogen. As a result, we recognized revenue relating to the upfront payment of \$2.0 million on a straight-line basis over the estimated period of performance, which was approximately one year based on the expected term of the research and development plan.

In July 2015, the collaboration and license agreement was amended to modify the conditions of the third research-based milestone. Additionally, the amendment extended the expected research term from 12 months to 14 months. We recognized the remaining upfront payment on a straight-line basis over the amended expected term. As of December 31, 2015, our period of performance was complete and the deferred revenue balance was zero.

In January 2015, May 2015, and September 2015, we earned research milestone payments under the collaboration and license agreement of \$0.1 million, \$0.3 million and \$0.3 million, respectively. We evaluated the contingent event-based payments under our collaboration and license agreement with Biogen and determined that the research milestone payments met the definition of substantive milestones. Accordingly, revenue for these achievements was recognized in the period the milestones were achieved and collectability was reasonably assured.

8. Related Party Transactions

We have entered into certain agreements with related parties in the ordinary course of business to license intellectual property and to procure administrative and research and development support services.

In September 2014, we entered into an agreement with Sanofi-Aventis Deutschland GmbH ("Sanofi Deutschland"), a contract manufacturing subsidiary of Sanofi, for the manufacture of certain drug substance requirements and other services to support our preclinical and clinical activities associated with the RG-012 program. Pursuant to this agreement, we may engage Sanofi Deutschland from time-to-time to manufacture RG-012 drug product on our behalf. Expenses incurred under the Sanofi agreement for services performed or out-of-pocket expenses were less than \$0.1 million and \$0.8 million for the three and six months ended June 30, 2016, respectively, compared to zero and \$0.4 million for the same periods in 2015.

In February 2015, we entered into a letter agreement with Alnylam Pharmaceuticals, Inc. ("Alnylam") pursuant to which we and Alnylam agreed to the financial terms for certain technology acquired by Alnylam within the licensed patent rights under our Amended and Restated License and Collaboration Agreement (the "Additional Patent Rights") with Alnylam and Ionis Pharmaceuticals, Inc. In addition to any royalties payable by us to Alnylam pursuant to the terms of the Amended and Restated License and Collaboration Agreement, we agreed to pay Alnylam an additional low single-digit royalty on net sales of certain products utilizing the Additional Patent Rights, with the exact royalty percentage payable being dependent on the total amount of net sales during the calendar year. We also agreed to pay Alnylam milestone payments on certain products utilizing the additional patent rights of up to \$33.0 million per product upon the achievement of certain regulatory milestone events. There was no activity under this agreement for the three or six months ended June 30, 2016.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The interim unaudited condensed financial statements and this Management's Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with the financial statements and notes thereto for the year ended December 31, 2015 and the related Management's Discussion and Analysis of Financial Condition and Results of Operations, both of which are contained in our Annual Report on Form 10-K for the year ended December 31, 2015, or Annual Report, filed with the Securities and Exchange Commission on February 23, 2016. Past operating results are not necessarily indicative of results that may occur in future periods.

FORWARD-LOOKING STATEMENTS

This quarterly report on Form 10-Q and the documents incorporated by reference herein may contain “forward-looking statements” within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below under Part II, Item 1A, “Risk Factors” in this quarterly report on Form 10-Q. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise. These statements, which represent our current expectations or beliefs concerning various future events, may contain words such as “may,” “will,” “expect,” “anticipate,” “intend,” “plan,” “believe,” “estimate” or other words indicating future results, though not all forward-looking statements necessarily contain these identifying words. Such statements may include, but are not limited to, statements concerning the following:

- the initiation, cost, timing, progress and results of, and our expected ability to undertake certain activities and accomplish certain goals with respect to our research and development activities, preclinical studies and clinical trials;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our product candidates;
- our strategic alliance partners’ election to pursue development and commercialization of any programs or product candidates that are subject to our collaboration and license agreements with such partners;
- our ability to attract collaborators with relevant development, regulatory and commercialization expertise;
- future activities to be undertaken by our strategic alliance partners, collaborators and other third parties;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize, and our expectations regarding future therapeutic and commercial potential with respect to our product candidates;
- the rate and degree of market acceptance of our product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the loss of key scientific or management personnel;
- our ability to successfully secure and deploy capital;
- our ability to satisfy our debt obligations;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act;
- the accuracy of our estimates regarding future expenses, future revenues, capital requirements and need for additional financing; and
- the risks and other forward-looking statements described under the caption “Risk Factors” under Part II, Item 1A of this quarterly report on Form 10-Q.

OVERVIEW

We are a biopharmaceutical company focused on discovering and developing first-in-class drugs that target *micro* RNAs to treat a broad range of diseases. We were formed in 2007 when Alnylam Pharmaceuticals, Inc. and Ionis Pharmaceuticals, Inc. contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting *micro* RNAs pursuant to a license and collaboration agreement. We have established strategic alliances with AstraZeneca AB and Sanofi to discover, develop and commercialize *micro* RNA therapeutics. Under these strategic alliances, we are eligible to receive approximately \$900.0 million in aggregate milestone payments upon successful commercialization

of *micro* RNA therapeutics and royalties on net sales for the programs contemplated by our agreements. These payments include up to \$107.8 million upon achievement of preclinical and investigational new drug, or IND, milestones, up to \$128.0 million upon achievement of clinical development milestones, up to \$180.0 million upon achievement of regulatory milestones and up to \$490.0 million upon achievement of commercialization milestones.

micro RNAs are naturally occurring ribonucleic acid, or RNA, molecules that play a critical role in regulating key biological pathways. Scientific research has shown that the improper balance, or dysregulation, of *micro* RNAs is directly linked to many diseases. To date, approximately 500 *micro* RNAs have been identified in humans, each of which is believed to interact with a specific set of genes that control key aspects of cell biology. Since most diseases are multi-factorial and involve multiple targets in a pathway, the ability to modulate gene networks by targeting a single *micro* RNA provides a new therapeutic approach for treating complex diseases.

RNA plays an essential role in the process used by cells to encode and translate genetic information from DNA to proteins. RNA is comprised of subunits called nucleotides and is synthesized from a DNA template by a process known as transcription. Transcription generates different types of RNA, including messenger RNAs that carry the information for proteins in the sequence of their nucleotides. In contrast, *micro* RNAs are RNAs that do not code for proteins but rather are responsible for regulating gene expression by affecting the translation of target messenger RNAs. By interacting with many messenger RNAs, a single *micro* RNA can regulate several genes that are instrumental for the normal function of a biological pathway.

We believe that *micro* RNA therapeutics have the potential to become a new and major class of drugs with broad therapeutic application for the following reasons:

- *micro* RNAs, until recently, have not been a focus of pharmaceutical research;
- *micro* RNAs play a critical role in regulating biological pathways by controlling the translation of many target genes;
- *micro* RNA therapeutics target entire disease pathways which may result in more effective treatment of complex multi-factorial diseases; and
- *micro* RNA therapeutics may be synergistic with other therapies because of their different mechanism of action.

We believe we have assembled the leading position in the *micro* RNA field, including expertise in *micro* RNA biology and oligonucleotide chemistry, a broad intellectual property estate, relationships with key opinion leaders and a disciplined drug discovery and development process. We refer to these assets as our *micro* RNA product platform. We are using our *micro* RNA product platform to develop chemically modified, single-stranded oligonucleotides that we call anti-miRs to modulate *micro* RNAs and return diseased cells to their healthy state. We believe *micro* RNAs may be transformative in the field of drug discovery and that anti-miRs may become a new and major class of drugs with broad therapeutic application, much like small molecules, biologics and monoclonal antibodies. In addition to our *micro* RNA product platform, we have established Regulus *micro* MarkersSM, a division focused on identifying *micro* RNAs as biomarkers of human disease to support our therapeutic pipeline, collaborators and strategic partners. Regulus *micro* MarkersSM utilizes a clinically-validated, highly reproducible technology platform to identify *micro* RNAs as potential biomarkers for disease and we control key intellectual property and know-how related to the division. We believe that *micro* RNA biomarkers may be used to select optimal patient segments in clinical trials and to monitor disease progression or relapse. We believe these *micro* RNA biomarkers can be applied toward drugs that we develop and drugs developed by other companies with which we partner or collaborate. We have completed a research collaboration with Biogen focused on the discovery of *micro* RNAs as biomarkers for multiple sclerosis and have also completed research for another leading, commercial-stage pharmaceutical company to explore *micro* RNAs as biomarkers for specific patient populations. We also maintain several academic research collaborations focused on the identification of *micro* RNAs as biomarkers in multiple disease areas.

Development Stage Pipeline

We currently have three programs in clinical development. Our most advanced program, RG-101, is a GalNAc-conjugated anti-miR targeting miR-122, a host factor for the hepatitis C virus, or HCV, infection. Our second program is RG-012, an anti-miR targeting *micro* RNA-21 for the treatment of Alport syndrome, a life-threatening kidney disease driven by genetic mutations, currently with no approved therapy available. Our third program, under our strategic alliance with AstraZeneca is RG-125, a GalNAc-conjugated anti-miR targeting *micro* RNA-103/107 for the treatment of nonalcoholic steatohepatitis, or NASH, in patients with type 2 diabetes/pre-diabetes. AstraZeneca commenced clinical development of RG-125 in December 2015.

RG-101: We are currently evaluating RG-101 in several Phase I/II studies.

- In August 2015, we initiated a Phase II study investigating RG-101 designed to evaluate a shortened, four-week treatment regimen containing a subcutaneous administration of 2 mg/kg of RG-101 at Day 1 and Day 29, in combination with oral direct-acting antiviral agents Harvoni®, Olysio®, and Daklinza® for 28 days. In June 2016, we announced positive top-line results from the primary endpoint analysis of this clinical study:

Number and Percentage of Patients with Response at Various Timepoints

Time Since Treatment Completion	RG-101 + Harvoni®	RG-101 + Olysio®	RG-101 + Daklinza™
Week 12	27/27 (100%)	26/27 (96.3%)	22/24 (91.7%)*
Week 16	21/21 (100%)	19/20 (95.0%)	20/22 (90.9%)
Week 20	14/14 (100%)	13/15 (86.7%)	13/13 (100%)
Week 24	10/10 (100%)	8/10 (80.0%)	8/9 (88.9%)

**One patient missed the Week 12 visit. Viral load results for this patient at Week 8 and 16 were collected and indicate that the patient was a responder at both time points.*

The results from this interim analysis demonstrated significant virologic response through 24 weeks of follow-up. RG-101 plus Harvoni continued to demonstrate 100% response rates. As previously reported, the combination of RG-101 plus either Olysio or Daklinza monotherapies have seen small numbers of viral relapse. The results reported include four new relapses: two in the Olysio arm (weeks 20 and 32) and two in the Daklinza arm (weeks 12 and 24). RG-101 in combination with four weeks of oral DAA therapy has been generally well tolerated with the majority of adverse events considered mild or moderate, and with no study discontinuations. Commonly reported adverse events, or AEs, included fatigue, headache, and injection site reactions. In addition, three out of 79 patients had experienced severe adverse events, or SAEs, as of the time of this analysis.

- In November 2015, we entered into a clinical trial collaboration and formulation agreement with GSK LLC. In Q1 2016, we initiated a Phase II study evaluating the potential to achieve sustained viral responses post treatment with a single subcutaneous administration of RG-101 in combination with daily oral administrations of GSK2878175, a non-nucleoside NS5B polymerase inhibitor, for up to 12 weeks in treatment-naïve patients chronically infected with HCV genotypes 1 and 3. Concurrently, GSK had initiated the development of a long-acting parenteral formulation for injection, or LAP, of GSK2878175 which could improve patient compliance through reduced dosing intervals and potentially extend opportunities for HCV therapeutic intervention. We expect to report interim safety and efficacy data from the GSK Phase II study before the end of 2016.
- In May 2016, we expanded the clinical trial collaboration agreement with GSK to conduct a multi-centered, randomized, dose-ranging Phase II study evaluating the combination of RG-101 and GSK's LAP formulation of GSK2878175 as a potential single-visit cure in patients chronically infected with HCV. This study will be conducted outside the United States and is planned to begin in the fourth quarter of 2016. Based on predicted enrollment rates, we expect interim results from this expanded collaboration to be available in the second half of 2017, enabling a potential initiation of a pivotal study in late 2017. As with the initial collaboration, both parties will contribute to the costs associated with the study. Neither we nor GSK has any further obligations or commitments to each other beyond this expanded clinical collaboration agreement.
- In January 2016, we initiated a multi-center, open label, non-randomized Phase I study to compare the safety, tolerability, pharmacokinetics, and pharmacodynamics of 2 mg/kg of RG-101 in subjects with severe renal insufficiency or end-stage renal disease (ESRD) to healthy control subjects, and further explore RG-101 in hepatitis C infected subjects with severe renal insufficiency or ESRD. The Phase I study has three treatment arms (n=24): (i) healthy volunteers (n=8); (ii) patients with severe renal impairment or ESRD (n=8); and (iii) HCV patients with severe renal impairment or ESRD (n=8). Enrollment was completed in the second quarter of 2016, and we anticipate reporting additional safety and efficacy data from the HCV/severe renal impairment or ESRD arm in the second half of 2016.
- In June 2016, we received verbal notice from the U.S. Food and Drug Administration, or FDA, that our IND for RG-101 for the treatment of chronic HCV infection has been placed on clinical hold. The FDA initiated the clinical

hold after a second patient experienced an SAE of jaundice. This SAE occurred in an HCV patient with end-stage renal disease on dialysis enrolled in our on-going Phase I US study 117 days after receiving a single dose of RG-101. Timelines for our three on-going studies of RG-101 are not expected to be impacted as all patients have been enrolled and completed their dosing of RG-101 and will continue with protocol scheduled visits. In July 2016, we received a formal clinical hold letter from the FDA requesting the following from us: detailed safety data analysis from preclinical and clinical studies; exploration of potential mechanisms of hepatotoxicity in non-clinical models; review and input from independent hepatotoxicity experts; additional PK data from the US Phase I study; and a risk/benefit assessment for the proposed therapeutic regimen containing RG-101. We anticipate submitting the necessary information by early Q4 2016. The FDA will notify us of its decision within 30 days of receipt of the complete response to the issues. We plan to work diligently with the FDA to seek the release of the clinical hold.

RG-012: In 2015, we completed a Phase I study to evaluate the safety, tolerability and pharmacokinetics of subcutaneous dosing of RG-012 in healthy volunteers. Forty healthy volunteer subjects were enrolled in this first-in-human, single ascending dose study. RG-012 was well-tolerated and there were no serious adverse events reported. We also continue to enroll Alport syndrome patients in our global ATHENA natural history of disease study, which is designed to characterize the natural decline of renal function (as measured by established renal markers) in Alport syndrome patients over time. The data from the ATHENA study provided the clinical basis for the design of a Phase II proof-of-concept study to monitor the therapeutic effect of RG-012 on the decline in renal function in patients with Alport syndrome. We plan to initiate a Phase II proof-of-concept study evaluating the efficacy of RG-012 in Alport syndrome patients in mid-2016.

RG-125: AstraZeneca initiated a Phase I study evaluating RG-125 in humans in December 2015, earning us a \$10.0 million milestone from the collaboration. AstraZeneca is responsible for all future development for RG-125.

We are advancing our preclinical portfolio towards clinical development in renal, hepatic, and central nervous system diseases both independently and with our strategic alliance partners Sanofi and AstraZeneca, and anticipate nominating a new clinical candidate by the end of 2016.

FINANCIAL OPERATIONS OVERVIEW

Revenue

Our revenues generally consist of upfront payments for licenses or options to obtain licenses in the future, milestone payments and payments for other research services under strategic alliance and collaboration agreements.

In the future, we may generate revenue from a combination of license fees and other upfront payments, payments for research and development services, milestone payments, product sales and royalties in connection with strategic alliances. We expect that any revenue we generate will fluctuate from quarter-to-quarter as a result of the timing of our achievement of preclinical, clinical, regulatory and commercialization milestones, if at all, the timing and amount of payments relating to such milestones and the extent to which any of our products are approved and successfully commercialized by us or our strategic alliance partners. If our strategic alliance partners do not elect or otherwise agree to fund our development costs pursuant to our strategic alliance agreements, or we or our strategic alliance partners fail to develop product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenues, and our results of operations and financial position would be adversely affected.

Research and development expenses

Research and development expenses consist of costs associated with our research activities, including our drug discovery efforts, the development of our therapeutic programs, and our Regulus *micro* Markers SM division. Our research and development expenses include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, contract manufacturing organizations, or CMOs, other clinical trial related vendors, consultants and our scientific advisors;
- license fees; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

We expense research and development costs as incurred. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received.

To date, we have conducted research on many different *micro* RNAs with the goal of understanding how they function and identifying those that might be targets for therapeutic modulation. At any given time we are working on multiple targets, primarily within our therapeutic areas of focus. Our organization is structured to allow the rapid deployment and shifting of resources to focus on the best known targets based on our ongoing research. As a result, in the early phase of our development programs, our research and development costs are not tied to any specific target. However, we are currently spending the vast majority of our research and development resources on our lead development programs.

Since our conversion to a corporation in January 2009, we have grown from 15 research and development personnel to 77 and have spent a total of approximately \$229.0 million in research and development expenses through June 30, 2016 .

We expect our research and development expenses to increase for the foreseeable future as we continue to conduct our ongoing clinical studies, initiate additional clinical studies and advance our preclinical research programs toward the clinic, including other IND-enabling activities. The process of conducting clinical trials and preclinical studies necessary to obtain regulatory approval is costly and time consuming. We, or our strategic alliance partners, may never succeed in achieving marketing approval for any of our product candidates. The probability of success for each product candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability. Under our strategic alliance with Sanofi, we are responsible for the development of product candidates through proof-of-concept, after which time Sanofi would be responsible for the costs of clinical development and commercialization and all related costs, in the event it exercises its option to such program. Under our strategic alliance agreement with AstraZeneca, we are responsible for certain research and development activities with respect to each alliance target under a mutually agreed upon research and development plan until the earlier to occur of acceptance of an IND application (or its foreign equivalent) in a major market or the end of the research term under the agreement. We also have several independent programs for which we are responsible for all of the research and development costs, unless and until we partner any of these programs in the future.

Successful development of future product candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We anticipate we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to our ability to maintain or enter into new strategic alliances with respect to each program or potential product candidate, the scientific and clinical success of each future product candidate, as well as ongoing assessments as to each future product candidate's commercial potential. We will need to raise additional capital and may seek additional strategic alliances in the future in order to advance our various programs.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, legal, business development and support functions. Other general and administrative expenses include allocated facility-related costs not otherwise included in research and development expenses and professional fees for auditing, tax and legal services. We expect that general and administrative expenses will increase in the future as we expand our operating activities and incur additional costs associated with being a publicly-traded company. These costs will likely include legal fees, Sarbanes-Oxley compliance and other accounting fees and directors' and officers' liability insurance premiums.

Other income (expense), net

Other income (expense) consists primarily of interest income and expense and various income or expense items of a non-recurring nature. We earn interest income from interest-bearing accounts and money market funds for cash and cash equivalents and marketable securities, such as interest-bearing bonds, for our short-term investments. Commencing in June 2016, interest expense is primarily attributable to interest charges associated with borrowings under our term loan. Historically, we recorded periodic gains and losses from changes in value of a convertible note payable until its conversion into common stock in January 2015.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

There have been no significant changes to our critical accounting policies since December 31, 2015 . For a description of critical accounting policies that affect our significant judgments and estimates used in the preparation of our consolidated financial statements, refer to Item 7 in Management's Discussion and Analysis of Financial Condition and Results of

Operations and Note 1 to our financial statements contained in our Annual Report and Note 1 to our condensed financial statements contained in this quarterly report on Form 10-Q.

RESULTS OF OPERATIONS

Comparison of the three and six months ended June 30, 2016 and 2015

The following table summarizes our results of operations for the three and six months ended June 30, 2016 and 2015 (in thousands):

	Three months ended June 30,		Six months ended June 30,	
	2016	2015	2016	2015
Revenue under strategic alliances and collaborations	\$ 483	\$ 3,834	\$ 972	\$ 8,034
Research and development expenses	18,007	19,201	34,772	32,628
General and administrative expenses	3,664	5,814	8,767	9,458
Loss from valuation of convertible note payable	—	—	—	(1,811)

Revenue under strategic alliances and collaborations

Our revenues are generated from ongoing strategic alliance and collaborations, and generally consist of upfront payments for licenses or options to obtain licenses in the future, milestone payments and payments for other research services. The following table summarizes our total revenues for the periods indicated (in thousands):

	Three months ended June 30,		Six months ended June 30,	
	2016	2015	2016	2015
AstraZeneca	\$ 465	\$ 3,066	\$ 936	\$ 6,648
Sanofi	18	18	36	36
Biogen	—	750	—	1,350
Total revenues under strategic alliances and collaborations	\$ 483	\$ 3,834	\$ 972	\$ 8,034

Revenue under strategic alliances was \$0.5 million and \$1.0 million for the three and six months ended June 30, 2016, respectively, compared to \$3.8 million and \$8.0 million for the three and six months ended June 30, 2015, respectively.

Revenue under the AstraZeneca collaboration and license agreement decreased to \$0.5 million and \$0.9 million for the three and six months ended June 30, 2016, respectively, compared to \$3.1 million and \$6.6 million for the same periods in 2015. Revenue recognized in the three and six months ended June 30, 2016 related to the amortization of upfront payments over our estimated period of performance. Revenue of \$2.6 million and \$3.2 million was recognized under the January 2015 letter agreement for the three and six months ended June 30, 2015, respectively. As of December 31, 2015, the Company's obligations under the letter agreement were complete. In March 2015, we earned a \$2.5 million preclinical milestone payment for the clinical candidate selection of RG-125, a GalNAc-conjugated anti-miR targeting microRNA-103/107 for the treatment of NASH in patients with type 2 diabetes/pre-diabetes.

Revenue recognized from our collaboration and license agreement with Biogen decreased to zero for the three and six months ended June 30, 2016, compared to \$0.8 million and \$1.4 million for the same periods in 2015, as a result of the completion of our performance under the collaboration and license agreement as of September 2015.

As of June 30, 2016, we had \$2.3 million of deferred revenue, which consisted of payments received through our strategic alliances that have not yet been recognized in accordance with our revenue recognition policies.

Research and development expenses

Research and development expenses were \$18.0 million and \$34.8 million for the three and six months ended June 30, 2016, respectively, compared to \$19.2 million and \$32.6 million for the three and six months ended June 30, 2015, respectively.

The decrease of \$1.2 million for the three months ended June 30, 2016 compared to the three months ended June 30, 2015 was driven by non-recurring severance charges of \$1.3 million in June 2015. The increase of \$2.2 million for the six months

ended June 30, 2016 compared to the six months ended June 30, 2015 was driven by a net increase in our aggregate clinical trial program costs of \$5.5 million, offset by a \$3.1 million decrease in non-cash stock-based compensation expense and the non-recurring severance charges for the six months ended June 30, 2016, compared to the same period in 2015.

Clinical trial costs for RG-101 increased by \$1.7 million and \$7.2 million for the three and six months ended June 30, 2016, respectively, compared to the same periods in 2015. These increases were due to incremental costs incurred associated with Phase II studies for RG-101. Clinical trial program costs for RG-012 increased by \$1.8 million and \$2.5 million for the three and six months ended June 30, 2016, respectively, compared to the same periods in 2015. These increases were due to costs associated with our global ATHENA natural history of disease study and manufacturing costs for RG-012. These increases were partially offset by a decrease in preclinical study costs for RG-125 of \$2.9 million and \$4.2 million for the three and six months ended June 30, 2016, respectively, compared to the same periods in 2015. Upon completion of the technology transfer to AstraZeneca in December 2015, our development obligations were completed, and we anticipate no further research and development expenses related to the future development of RG-125.

We expect our research and development expenses to increase for the foreseeable future as we continue to conduct our ongoing clinical studies, initiate additional clinical studies and advance our preclinical research programs toward the clinic, including other IND-enabling activities.

General and administrative expenses

General and administrative expenses were \$3.7 million and \$8.8 million for the three and six months ended June 30, 2016, respectively, compared to \$5.8 million and \$9.5 million for the three and six months ended June 30, 2015, respectively. This decrease was principally driven by a non-recurring severance charge of \$3.3 million in June 2015, offset by an increase in personnel costs, including non-cash stock based compensation, of \$1.0 million and \$2.3 million for the three and six months ended June 30, 2016, respectively, compared to the same periods in 2015. We expect our general and administrative expenses to increase for the foreseeable future as we expand our operating activities and incur additional costs associated with being a publicly-traded company.

Loss from valuation of convertible note payable

On January 29, 2015, the principal amount outstanding under a \$5.4 million convertible note issued by us to Glaxo Group Limited was converted into 1,356,738 shares of our common stock at a conversion price of \$4.00 per share. Upon conversion, we recorded a loss from the change in value of the convertible note payable of \$1.8 million for the six months ended June 30, 2015.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception through June 30, 2016, we have received \$85.1 million principally from upfront payments, research funding and preclinical milestones from our strategic alliances and collaborations, \$257.1 million from the sale of our equity and convertible debt securities (including \$70.0 million in net proceeds from our initial public offering and concurrent private placement of our common stock in October 2012, \$45.8 million in net proceeds from our public offering in July 2013 and \$76.3 million in net proceeds from our public offering in November 2014) and \$19.8 million in net proceeds from our June 2016 secured term loan.

As of June 30, 2016, we had \$108.0 million in cash, cash equivalents and short-term investments, including \$0.5 million in restricted cash. The following table shows a summary of our cash flows for the six months ended June 30, 2016 and 2015 (in thousands):

	Six months ended June 30,	
	2016	2015
	(unaudited)	
Net cash (used in) provided by:		
Operating activities	\$ (26,275)	\$ (21,015)
Investing activities	16,991	2,935
Financing activities	20,364	1,837
Total	<u>\$ 11,080</u>	<u>\$ (16,243)</u>

Operating activities

Net cash used in operating activities was \$26.3 million for the six months ended June 30, 2016, compared to \$21.0 million for the six months ended June 30, 2015. The increase in net cash used in operating activities was attributable to an increase in net loss of \$6.8 million for the six months ended June 30, 2016, compared to the same period in 2015, and a \$5.1 million reduction in non-cash charges, including stock-based compensation and changes in the value of our convertible note payable.

The increase in net cash used in operating activities was partially offset by changes in working capital, which resulted in net cash provided by operating activities of \$8.7 million for the six months ended June 30, 2016, compared to net cash provided by operating activities of \$2.1 million for the six months ended June 30, 2015. This change was principally due to the receipt of \$10.0 million from AstraZeneca in February 2016 for a milestone achieved in December 2015.

Investing activities

Net cash provided by investing activities for the periods presented primarily related to the net of purchases, sales and maturities of investments used to fund the day-to-day needs of our business. We invest cash in excess of our immediate operating requirements in such a way that maturity is staggered to optimize our return on investment while satisfying our liquidity needs. Net cash provided by the net sales and maturities of short-term investments was \$17.3 million for the six months ended June 30, 2016, compared to \$3.4 million for the six months ended June 30, 2015. Net cash used for purchases of property and equipment was \$0.3 million for the six months ended June 30, 2016, compared to \$0.4 million for the six months ended June 30, 2015.

Financing activities

Net cash provided by financing activities was \$20.4 million for the six months ended June 30, 2016, compared to \$1.8 million for the six months ended June 30, 2015. The increase in net cash provided by financing activities was attributable to receipt of proceeds from the \$20.0 million Term A Loan. The increase in net cash provided by financing activities was partially offset by a decrease in proceeds from the exercise of common stock options of \$1.4 million for the six months ended June 30, 2016, compared to the same period in 2015.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

As of June 30, 2016, there have been no material changes, outside of the ordinary course of business, in our outstanding contractual obligations from those disclosed within "Management's Discussion and Analysis of Financial Condition and Results of Operations", as contained in our Annual Report, other than the following:

On June 17, 2016, we entered into a loan and security agreement with Oxford Finance, LLC, or Oxford, pursuant to which Oxford agreed to lend us up to \$30.0 million, issuable in two separate term loans of \$20.0 million (the Term A Loan) and \$10.0 million (the Term B Loan). We collectively refer to the Term A Loan and the Term B Loan as the Term Loans. On June 22, 2016, we received \$20.0 million in proceeds from the Term A Loan, net of debt issuance costs.

The Term A Loan matures on June 1, 2020. Repayment of the Term A Loan will be interest-only through June 1, 2018, followed by 24 months of principal and interest payments. The Term A Loan bears interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S. Dollar LIBOR rate on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44%.

Off-Balance Sheet Arrangements

As of June 30, 2016, we did not have any off-balance sheet arrangements.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Some of the securities that we invest in have market risk in that a change in prevailing interest rates may cause the principal amount of the marketable securities to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash, cash equivalents and short-term investments. We invest our excess cash primarily in commercial paper and debt instruments of financial institutions, corporations, U.S. government-sponsored agencies and the U.S. Treasury. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our marketable securities without significantly increasing risk.

Additionally, we established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Because of the short-term maturities of our cash equivalents and marketable securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our marketable securities.

We also have interest rate exposure as a result of our Term A Loan. As of June 30, 2016, the outstanding principal amount of the Term A Loan was \$20.0 million. The Term A Loan bears interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S. Dollar LIBOR rate reported in *The Wall Street Journal* on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44%. Changes in the U.S. Dollar LIBOR rate may therefore affect our interest expense associated with the Term A Loan.

If a 10% change in interest rates were to have occurred on June 30, 2016, this change would not have had a material effect on the fair value of our investment portfolio or our interest expense as of that date.

ITEM 4. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of June 30, 2016, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and our principal financial and accounting officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of June 30, 2016.

Changes in Internal Control Over Financial Reporting

An evaluation was also performed under the supervision and with the participation of our management, including our principal executive officer and our principal financial and accounting officer, of any change in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. That evaluation did not identify any change in our internal control over financial reporting that occurred during our latest fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

None.

ITEM 1A. RISK FACTORS

You should carefully consider the following risk factors, as well as the other information in this report, before deciding whether to purchase, hold or sell shares of our common stock. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You

should consider all of the factors described when evaluating our business. The risk factors set forth below that are marked with an asterisk () did not appear as separate risk factors in, or contain changes to the similarly titled risk factors included in Item 1A of our Annual Report. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline.*

RISKS RELATED TO OUR FINANCIAL CONDITION AND NEED FOR ADDITIONAL CAPITAL

We have a limited operating history, have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. *

We are a biopharmaceutical company, formed in 2007, with a limited operating history. Since inception, our operations have been primarily limited to organizing and staffing our company, acquiring and in-licensing intellectual property rights, developing our *micro* RNA product platform, undertaking basic research around *micro* RNA targets and conducting preclinical and clinical studies for our initial programs. We have initiated clinical development of RG-101 and RG-012, and AstraZeneca has initiated clinical development of RG-125 under our strategic alliance, however, we have not yet obtained regulatory approval for any product candidates. Consequently, any predictions about our future success or viability, or any evaluation of our business and prospects, may not be accurate.

We have incurred losses in each year since our inception in September 2007. Our net losses were \$21.1 million and \$21.0 million for the three months ended June 30, 2016 and 2015, respectively, and \$42.3 million and \$35.5 million for the six months ended June 30, 2016 and 2015, respectively. As of June 30, 2016, we had an accumulated deficit of \$233.8 million.

We have devoted most of our financial resources to research and development, including our preclinical and clinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt and from revenue received from our strategic alliance partners. We have a strategic alliance with Sanofi relating to the development of our miR-21 programs for HCC and kidney fibrosis and our miR-221/222 program for oncology indications and with AstraZeneca to develop metabolic and oncology programs, including development of RG-125 for NASH. Under our agreement with Sanofi, Sanofi has an option to obtain exclusive worldwide licenses for the development, manufacture and commercialization of potential product candidates selected from our programs. If Sanofi exercises its option to obtain a license to develop, manufacture and commercialize any such product candidate, it will assume responsibility for funding and conducting further clinical development and commercialization activities for such product candidate. However, if Sanofi does not exercise its option within the timeframes that we expect, or at all, we will be responsible for funding further development of the applicable product candidate and may not have the resources to do so unless we are able to enter into another strategic alliance for such product candidate. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to obtain funding through equity or debt financings, strategic alliances or grants. We have initiated clinical development of RG-101 and RG-012, and AstraZeneca has initiated clinical development of RG-125, however, it will be several years, if ever, before we or our strategic alliance partners have a product candidate ready for commercialization. Even if we or our strategic alliance partners successfully obtain regulatory approval to market a product candidate, our revenues will also depend upon the size of any markets in which our product candidates have received market approval, and our ability to achieve sufficient market acceptance and adequate market share for our products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we: continue our research and preclinical and clinical development of our product candidates, both independently and under our strategic alliance agreements; seek to identify additional *micro* RNA targets and product candidates; acquire or in-license other products and technologies; continue with clinical development of our product candidates; seek marketing approvals for our product candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; maintain, expand and protect our intellectual property portfolio; hire additional clinical, regulatory, research and administrative personnel; and create additional infrastructure to support our operations as a publicly traded company and our product development and planned future commercialization efforts.

We have never generated any revenue from product sales and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic alliance partners, to successfully complete the development of, obtain the necessary regulatory approvals for and commercialize product candidates. We do not anticipate generating revenues from sales of products for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on our success in:

- identifying and validating new *micro* RNAs as therapeutic targets;
- completing our research and preclinical development of product candidates;
- initiating and completing clinical trials for product candidates;
- seeking and obtaining marketing approvals for product candidates that successfully complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties;
- launching and commercializing product candidates for which we obtain marketing approval, with an alliance partner or, if launched independently, successfully establishing a sales force, marketing and distribution infrastructure;
- maintaining, protecting and expanding our intellectual property portfolio; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of increased expenses and when we will be able to achieve or maintain profitability, if ever. In addition, our expenses could increase beyond expectations if we are required by the FDA or foreign regulatory agencies to perform studies and trials in addition to those that we currently anticipate.

Even if one or more of the product candidates that we independently develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We may need to raise additional capital, which may not be available on acceptable terms, or at all.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect our research and development expenses to substantially increase in connection with our ongoing activities, particularly as we advance our product candidates towards or through clinical trials. We will need to raise additional capital to support our operations and such funding may not be available to us on acceptable terms, or at all.

As we move our lead compounds through toxicology and other preclinical studies, also referred to as nonclinical studies, required to file an IND, and as we conduct clinical development of RG-101, RG-012 and any other future product candidates, we may have adverse results requiring mitigation strategies that may cause us to consume additional capital. Additionally, our strategic alliance partners may not elect to pursue the development and commercialization of any of our *micro* RNA product candidates that are subject to their respective strategic alliance agreements with us. Any of these events may increase our development costs more than we expect. We may need to raise additional capital or otherwise obtain funding through additional strategic alliances if we choose to initiate clinical trials for new product candidates other than programs currently partnered. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, future product candidates.

If we are required to secure additional financing, such additional fundraising efforts may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize future product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back or discontinue the development or commercialization of any future product candidates;
- seek strategic alliances for research and development programs at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or
- relinquish or license on unfavorable terms, our rights to technologies or any future product candidates that we otherwise would seek to develop or commercialize ourselves.

If we are required to conduct additional fundraising activities and we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing development and commercialization efforts, which will have a material adverse effect on our business, operating results and prospects.

Payments under the instruments governing our indebtedness may reduce our working capital. In addition, a default under our loan and security agreement could cause a material adverse effect on our financial position.*

In June 2016, we entered into a loan and security agreement with Oxford. Under the terms of the loan agreement, Oxford initially provided us with a Term A Loan of \$20.0 million, with an additional \$10.0 million Term B Loan available to us upon the achievement of a milestone until the earlier of 60 days after the achievement of the milestone or March 31, 2017, subject to the non-occurrence of a prior event of default. Our obligations under the loan agreement are secured by a first priority security interest in substantially all of our current and future assets, other than our intellectual property. We have also agreed not to encumber our intellectual property assets, except as permitted by the loan agreement. All of the Term Loans mature on June 1, 2020 and will be interest-only through June 1, 2018, followed by 24 months of principal and interest payments. Payments under the loan agreement could result in a significant reduction of our working capital.

The loan agreement requires us, and any debt arrangements we may enter into in the future may require us, to comply with various covenants that limit our ability to, among other things:

- dispose of assets;
- complete mergers or acquisitions;
- incur indebtedness;
- encumber assets;
- pay dividends or make other distributions to holders of our capital stock;
- make specified investments; and
- engage in transactions with our affiliates.

These restrictions could inhibit our ability to pursue our business strategies. If we default under our obligations under the loan agreement, the lender could proceed against the collateral granted to it to secure our indebtedness or declare all obligation under the loan agreement to be due and payable. In certain circumstances, procedures by the lenders could result in a loss by us of all of our equipment and inventory, which are included in the collateral granted to the lenders. If any indebtedness under the loan agreement were to be accelerated, there can be no assurance that our assets would be sufficient to repay in full that indebtedness. In addition, upon any distribution of assets pursuant to any liquidation, insolvency, dissolution, reorganization or similar proceeding, the holders of secured indebtedness will be entitled to receive payment in full from the proceeds of the collateral securing our secured indebtedness before the holders of other indebtedness or our common stock will be entitled to receive any distribution with respect thereto.

We may incur additional indebtedness in the future. The debt instruments governing such indebtedness may contain provisions that are as, or more, restrictive than the provisions governing our existing indebtedness under the loan agreement. If we are unable to repay, refinance or restructure our indebtedness when payment is due, the lenders could proceed against the collateral or force us into bankruptcy or liquidation.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2012 Equity Incentive Plan, or the 2012 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2012 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31st of the preceding calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. In addition, we may grant or provide for the grant of rights to purchase shares of our common stock pursuant to our 2012 Employee Stock Purchase Plan, or the ESPP. The number of shares of our common stock reserved for issuance under the ESPP will automatically increase on January 1 of each calendar year by the lesser of 1% of the total number of shares of our common stock outstanding on December 31st of the preceding calendar year and 500,000 shares, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Any such increase, of the maximum amount or a lesser amount, may cause our stockholders to experience additional dilution, which could cause our stock price to fall. Currently, we plan to register the increased number of shares available for issuance under the 2012 Plan and the ESPP each year.

In addition, we have adopted an Inducement Plan pursuant to which our management may grant stock options exercisable for up to an aggregate of 1,000,000 shares of our common stock to new employees as inducements material to such new employees entering into employment with us. The number of shares which may be granted under the Inducement Plan may be increased in the future by our board of directors. In the event we grant options pursuant to our Inducement Plan, our stockholders may experience additional dilution, which could cause our stock price to fall.

RISKS RELATED TO THE DISCOVERY AND DEVELOPMENT OF PRODUCT CANDIDATES

The FDA has placed a clinical hold on RG-101, our most advanced compound under development, after a second patient experienced a serious adverse event of jaundice in our on-going Phase I study for the treatment of chronic HCV infection. Our business may be adversely affected if the clinical hold cannot be favorably resolved in a timely manner or if such regulatory concerns lead to more burdensome preclinical or clinical studies that cause significant delays or expense in developing our product candidates.*

In June 2016, the FDA placed a clinical hold on our RG-101 clinical program after a second patient experienced an SAE of jaundice. This SAE occurred in a HCV patient with end-stage renal disease on dialysis enrolled in our on-going Phase I U.S. study 117 days after receiving a single dose of RG-101. In accordance with the clinical hold, the FDA provided that no new dosing with RG-101 could be initiated in the United States. In July 2016, we received a formal clinical hold letter from the FDA requesting the following from us: detailed safety data analysis from preclinical and clinical studies; exploration of potential mechanisms of hepatotoxicity in non-clinical models; review and input from independent hepatotoxicity experts; additional PK data from the US Phase I study; and a risk/benefit assessment for the proposed therapeutic regimen containing RG-101. We anticipate submitting the necessary information by early Q4 2016. The FDA will notify us of its decision within 30 days of receipt of the complete response to the issues. It is possible that as the ongoing trials conclude, additional safety issues may be observed.

We cannot be certain whether or when the FDA will lift the clinical hold and allow us to pursue further development of RG-101 in the United States. If the FDA does not lift the clinical hold, our development timelines and our business may be adversely affected and our stock price may further decline. Further, even if the FDA lifts the clinical hold, or if the FDA or other regulatory agencies continue to express safety concerns after the hold is lifted, future preclinical or clinical studies involving RG-101 or combination regimens which include RG-101 may be more burdensome or include additional preclinical or clinical endpoints that are difficult to meet. In such instances, our progress in the development of these drug candidates may be significantly slowed and the associated costs may be significantly increased, adversely affecting our business.

The approach we are taking to discover and develop drugs is novel and may never lead to marketable products.

We have concentrated our therapeutic product research and development efforts on *micro* RNA technology, and our future success depends on the successful development of this technology and products based on our *micro* RNA product platform. Neither we nor any other company has received regulatory approval to market therapeutics targeting *micro* RNAs. The scientific discoveries that form the basis for our efforts to discover and develop product candidates are relatively new. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. If we do not successfully develop and commercialize product candidates based upon our technological approach, we may not become profitable and the value of our common stock may decline.

Further, our focus solely on *micro* RNA technology for developing drugs as opposed to multiple, more proven technologies for drug development increases the risks associated with the ownership of our common stock. If we are not successful in developing any product candidates using *micro* RNA technology, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to identify and implement successfully an alternative product development strategy.

We may not be successful in our efforts to identify or discover potential product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize *micro* RNA therapeutics. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our research methodology or that of our strategic alliance partners may be unsuccessful in identifying potential product candidates;

- potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval; or
- our strategic alliance partners may change their development profiles for potential product candidates or abandon a therapeutic area.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

Preclinical studies and clinical trials of our product candidates may not be successful. If we are unable to successfully complete preclinical studies and clinical trials of our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification and development of product candidates that target *micro* RNAs. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates.

The success of our product candidates will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection for future product candidates;
- establishing and maintaining manufacturing relationships with third parties or establishing our own manufacturing capability; and
- successfully commercializing our products, if and when approved, whether alone or in collaboration with others.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully complete the development of, or commercialize, our product candidates, which would materially harm our business.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of product candidates, we or our strategic alliance partners must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their products.

Events which may result in a delay or unsuccessful completion of clinical development include:

- delays in reaching an agreement with the FDA or other regulatory authorities on final trial design;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- our inability to adhere to clinical trial requirements directly or with third parties such as CROs;
- delays in obtaining required institutional review board approval at each clinical trial site;

- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to product side effects or disease progression;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

If we or our strategic alliance partners are required to conduct additional clinical trials or other testing of any product candidates beyond those that are currently contemplated, are unable to successfully complete clinical trials of any such product candidates or other testing, or if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we or our strategic alliance partners may:

- be delayed in obtaining marketing approval for our future product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as originally intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. Any inability to successfully complete preclinical and clinical development, whether independently or with our strategic alliance partners, could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties.

Any of our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

Adverse events, or AEs, caused by our product candidates could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval. Certain oligonucleotide therapeutics have shown injection site reactions and pro-inflammatory effects and may also lead to impairment of kidney or liver function. There is a risk that our future product candidates may induce similar AEs.

If AEs are observed in any clinical trials of our product candidates, including those that our strategic partners may develop under our alliance agreements, our or our partners' ability to obtain regulatory approval for product candidates may be negatively impacted.

Further, if any of our future products, if and when approved for commercial sale, cause serious or unexpected side effects, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us or our partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our future products and impair our ability to generate revenues from the commercialization of these products either by us or by our strategic alliance partners.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize a product candidate and we cannot, therefore, predict the timing of any revenue from a future product.

Neither we nor our strategic alliance partners can commercialize a product until the appropriate regulatory authorities, such as the FDA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee recommends restrictions on approval or recommends non-approval. In addition, we or our strategic alliance partners may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process.

Even if we obtain regulatory approval for a product candidate, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, drug product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, and adherence to commitments made in the NDA. If we or a regulatory agency discovers previously unknown problems with a product such as AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we or our partners fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our future products and generate revenues.

We may not be successful in obtaining or maintaining necessary rights to *micro* RNA targets, drug compounds and processes for our development pipeline through acquisitions and in-licenses.

Presently we have rights to the intellectual property, through licenses from third parties and under patents that we own, to modulate only a subset of the known *micro* RNA targets. Because our programs may involve a range of *micro* RNA targets, including targets that require the use of proprietary rights held by third parties, the growth of our business will likely depend in

part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we may collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and human resources, we intend to leverage our existing strategic alliance agreements and may enter into new strategic alliance agreements for the development and commercialization of our programs and potential product candidates in indications with potentially large commercial markets such as HCC, fibrosis and HCV, while focusing our internal development resources and any internal sales and marketing organization that we may establish on research programs and product candidates for selected markets, such as orphan diseases. As a result, we may forego or delay pursuit of opportunities with other programs or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic alliance, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

We will depend upon our strategic alliances for the development and eventual commercialization of certain *micro* RNA product candidates. If these strategic alliances are unsuccessful or are terminated, we may be unable to commercialize certain product candidates and we may be unable to generate revenues from our development programs.

We are likely to depend upon third party alliance partners for financial and scientific resources for the clinical development and commercialization of certain of our *micro* RNA product candidates. These strategic alliances will likely provide us with limited control over the course of development of a *micro* RNA product candidate, especially once a candidate has reached the stage of clinical development. For example, in our alliance with Sanofi, Sanofi has the option to obtain an exclusive worldwide license to develop, manufacture and commercialize product candidates upon the achievement of relevant endpoints in clinical trials. However, Sanofi is not under any obligation to exercise these options to progress any of our *micro* RNA development candidates. While each of AstraZeneca and Sanofi have development obligations with respect to programs that they may elect to pursue under their respective agreements, our ability to ultimately recognize revenue from these relationships will depend upon the ability and willingness of our alliance partners to successfully meet their respective responsibilities under our agreements with them. Our ability to recognize revenues from successful strategic alliances may be impaired by several factors including:

- an alliance partner may shift its priorities and resources away from our programs due to a change in business strategies, or a merger, acquisition, sale or downsizing of its company or business unit;
- an alliance partner may cease development in therapeutic areas which are the subject of our strategic alliances;
- an alliance partner may change the success criteria for a particular program or potential product candidate thereby delaying or ceasing development of such program or candidate;
- a significant delay in initiation of certain development activities by an alliance partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- an alliance partner could develop a product that competes, either directly or indirectly, with an alliance product;
- an alliance partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- an alliance partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- an alliance partner may exercise its rights under the agreement to terminate a strategic alliance;
- a dispute may arise between us and an alliance partner concerning the research, development or commercialization of a program or product candidate resulting in a delay in milestones, royalty payments or termination of a program and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- an alliance partner may use our proprietary information or intellectual property in such a way as to invite litigation from a third party or fail to maintain or prosecute intellectual property rights such that our rights in such property are jeopardized.

Specifically, with respect to termination rights, Sanofi may terminate the entire alliance or its current alliance target program for any or no reason upon 30 days' written notice to us. The agreement with Sanofi may also be terminated by either party for material breach by the other party, including a failure to comply with such party's diligence obligations that remains uncured after 120 days. The agreement with AstraZeneca may be terminated by either party in the event of the other party's material breach which remains uncured after 40 business days following notice thereof (or 30 business days in the case of nonpayment). In addition, AstraZeneca may terminate the agreement in its entirety for any reason upon 60 business days' written notice to us. Depending on the timing of any such termination, we may not be entitled to receive the option exercise fees or milestone payments, as these payments terminate with termination of the respective program or agreement.

If any of our alliance partners do not elect to pursue the development and commercialization of our *micro* RNA development candidates or if they terminate the strategic alliance, then, depending on the event:

- in the case of Sanofi, under certain circumstances, we may owe Sanofi royalties with respect to product candidates covered by our agreement with Sanofi that we elect to continue to commercialize, depending upon the stage of development at which such product commercialization rights reverted back to us, or additional payments if we license such product candidates to third parties;
- the development of our product candidates subject to the AstraZeneca agreement or the Sanofi agreement, as applicable, may be terminated or significantly delayed;

- our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate scarce resources to the development and commercialization of product candidates that were previously funded, or expected to be funded, by AstraZeneca or Sanofi, as applicable;
- we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of the AstraZeneca agreement or the Sanofi agreement, as applicable, including the reimbursement of third parties; and
- in order to fund further development and commercialization, we may need to seek out and establish alternative strategic alliances with third-party partners; this may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of one or more of our programs or increase our expenditures and seek additional funding by other means.

Any of these events would have a material adverse effect on our results of operations and financial condition.

We rely on third parties to conduct some aspects of our compound formulation, research and preclinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such formulation, research or testing.

We do not expect to independently conduct all aspects of our drug discovery activities, compound formulation research or preclinical studies of product candidates. We currently rely and expect to continue to rely on third parties to conduct some aspects of our preclinical studies and formulation development.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols for the trial.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the necessary preclinical studies to enable us or our strategic alliance partners to select viable product candidates for IND submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates.

We rely on third-party manufacturers to produce our preclinical and clinical product candidates, and we intend to rely on third parties to produce future clinical supplies of product candidates that we advance into clinical trials and commercial supplies of any approved product candidates.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to meet any product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to comply with cGMP and similar foreign standards;
- the inability to negotiate manufacturing or supply agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for raw materials, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell future product candidates in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for any raw materials that are currently purchased from a single source supplier;

- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver products under specified storage conditions and in a timely manner.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

We rely on limited sources of supply for the drug substance of product candidates and any disruption in the chain of supply may cause a delay in developing and commercializing these product candidates.

We have established manufacturing relationships with a limited number of suppliers to manufacture raw materials and the drug substance of any product candidate for which we are responsible for preclinical or clinical development. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain. As part of any marketing approval, a manufacturer and its processes are required to be qualified by the FDA prior to commercialization. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

In addition, if our alliance partners elect to pursue the development and commercialization of certain programs, we will lose control over the manufacturing of the product candidate subject to the agreement. For example, if Sanofi elects to develop and commercialize a product candidate targeting miR-21 or miR-221/222 for oncology indications or RG-012 for kidney fibrosis under its strategic alliance with us, Sanofi will be responsible for the manufacture of the product candidates for further clinical trials. Sanofi will be free to use a manufacturer of its own choosing or manufacture the product candidates in its own manufacturing facilities. In such a case, we will have no control over Sanofi's processes or supply chains to ensure the timely manufacture and supply of the product candidates. In addition, we will not be able to ensure that the product candidates will be manufactured under the correct conditions to permit the product candidates to be used in such clinical trials. AstraZeneca will have similar obligations to manufacture product candidates which it takes into clinical trials under its strategic alliance with us and we will face similar risks as to those product candidates.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to deliver the required commercial quantities of active pharmaceutical ingredients on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization.

As we scale-up manufacturing of product candidates and conduct required stability testing, product, packaging, equipment and process-related issues may require refinement or resolution in order to proceed with any clinical trials and obtain regulatory approval for commercial marketing. We may identify significant impurities, which could result in increased scrutiny by the regulatory agencies, delays in clinical programs and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for product candidates or any approved products.

We rely on third parties to conduct, supervise and monitor our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We or our strategic alliance partners rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. While we will have agreements governing their activities, we and our strategic alliance partners have limited influence over their actual performance. We control only certain aspects of our CROs' activities. Nevertheless, we or our strategic alliance partners are responsible for ensuring that each of our clinical trials are conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We, our alliance partners and our CROs are required to comply with the FDA's or other regulatory agency's GCPs for conducting, recording and reporting the results of IND-enabling studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA and other non-U.S. regulatory agencies enforce these GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our clinical trials will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of a potential drug product. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs will not be our employees, and we will not be able to control whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for such products and any product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We also rely on other third parties to store and distribute drug products for any clinical trials that we may conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, if approved, producing additional losses and depriving us of potential product revenue.

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

If we are unable to obtain or protect intellectual property rights related to our future products and product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our future products and product candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in patents with claims that cover the products in the United States or in other countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found; such prior art can invalidate a patent or prevent a patent from issuing based on a pending patent application. Even if patents do successfully issue, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims.

If the patent applications we hold or have in-licensed with respect to our programs or product candidates fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, future products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. A patent may be challenged through one or more of several administrative proceedings including post-grant challenges, re-examination or opposition before the U.S. PTO or foreign patent offices. For example, re-examination of, or oppositions to, patents owned by or licensed to us have previously been initiated, and while we believe these concluded proceedings did not result in a commercially relevant impact on the individual patents, any successful challenge of patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we or our strategic alliance partners may develop.

Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, in certain situations, if we and one or more third parties have filed patent applications in the United States and claiming the same subject matter, an administrative proceeding, known as an interference, can be initiated to determine which applicant is entitled to the patent on that subject matter. Such an interference proceeding provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications, or those of our alliance partners or licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party

does not offer us a license on commercially reasonable terms. Our defense of a patent or patent application in such a proceeding may not be successful and, even if successful, may result in substantial costs and distract our management and other employees.

In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Once the patent life has expired for a product, we may be open to competition from generic medications. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although each of our employees agrees to assign their inventions to us through an employee inventions agreement, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our strategic alliance partners are pursuing development candidates. For example, we are aware that Roche Innovation Center Copenhagen has patents and patent applications in the *micro* RNA therapeutics space, including patents and patent applications related to targeting *micro* RNAs, such as miR-122, for the treatment of disease. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit,

would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. For example, under our exclusive license agreement for Max-Planck-Innovation GmbH's proprietary technology and know-how covering *micro* RNA sequences, we are required to use commercially reasonable diligence to develop and commercialize a product and to satisfy specified payment obligations. If we fail to comply with our obligations under our agreement with Max-Planck-Innovation GmbH or our other license agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we, or our strategic alliance partners, would not be able to market products covered by the license. In addition, our exclusive license agreements with our founding companies, Alnylam and Ionis, provide us with rights to nucleotide technologies in the field of *micro* RNA therapeutics based on oligonucleotides that modulate *micro* RNAs. Some of these technologies, such as intellectual property relating to the chemical modification of oligonucleotides, are relevant to our product candidate development programs. If our license agreements with Alnylam or Ionis are terminated, or our business relationships with either of these companies or our other licensors are disrupted by events that may include the acquisition of either company, our access to critical intellectual property rights will be materially and adversely affected.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Our defense in a litigation may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend

against these claims. There is no guarantee of success in defending these claims, and if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

RISKS RELATED TO COMMERCIALIZATION OF PRODUCT CANDIDATES

The commercial success of our programs that are part of our strategic alliance agreements with Sanofi and AstraZeneca will depend in large part on the development and marketing efforts of our alliance partners. If our alliance partners are unable or unwilling to perform in accordance with the terms of our agreements, our potential to generate future revenue from these programs would be significantly reduced and our business would be materially and adversely harmed.

If or when Sanofi or AstraZeneca elects to pursue the development and commercialization of any of the *micro* RNA product candidates that are subject to their respective strategic alliance agreements with us, we will have limited influence and/or control over their approaches to development and commercialization. If Sanofi, AstraZeneca or any potential future strategic alliance partners do not perform in the manner that we expect or fail to fulfill their responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts related to product candidates we have licensed to such strategic alliance partners could be delayed or terminated. If we terminate any of our strategic alliances or any program thereunder due to a material breach by Sanofi or AstraZeneca, we have the right to assume the responsibility at our own expense for the development of the applicable *micro* RNA product candidates. Assuming sole responsibility for further development will increase our expenditures, and may mean we will need to limit the size and scope of one or more of our programs, seek additional funding and/or choose to stop work altogether on one or more of the affected product candidates. This could result in a limited potential to generate future revenue from such *micro* RNA product candidates and our business could be materially and adversely affected. Further, under certain circumstances, we may owe Sanofi or AstraZeneca, as applicable, royalties on any product candidate that we may successfully commercialize.

We face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. Our competitors may have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, drug products that are more effective or less costly than any product candidate that we may develop.

Most of our programs are targeted toward indications for which there are approved products on the market or product candidates in clinical development. We will face competition from other drugs currently approved or that will be approved in the future for the same therapeutic indications. Our ability to compete successfully will depend largely on our ability to leverage our experience in drug discovery and development to:

- discover and develop therapeutics that are superior to other products in the market;
- attract qualified scientific, product development and commercial personnel;
- obtain patent and/or other proprietary protection for our *micro* RNA product platform and future product candidates;
- obtain required regulatory approvals; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new therapeutics.

The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. We will not achieve our business plan if the acceptance of any of these products is inhibited by price competition or the reluctance of physicians to switch from existing drug products to our products, or if physicians switch to other new drug products or choose to reserve our future products for use in limited circumstances. The inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, financial condition and prospects.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or discovering, developing and commercializing product candidates before we do, which would have a material adverse impact on our business.

The commercial success of our product candidates will depend upon the acceptance of these product candidates by the medical community, including physicians, patients and healthcare payors.

The degree of market acceptance of any product candidates will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and healthcare payors;
- the prevalence and severity of any AEs;
- limitations or warnings contained in the FDA-approved label for such products;
- availability of alternative treatments;
- pricing and cost-effectiveness;
- the effectiveness of our or any collaborators' sales and marketing strategies;
- our ability to obtain hospital formulary approval;
- our ability to obtain and maintain sufficient third party coverage or adequate reimbursement; and
- the willingness of patients to pay out-of-pocket in the absence of third party coverage.

Unless other formulations are developed in the future, we expect our compounds to be formulated in an injectable form. Injectable medications may be disfavored by patients or their physicians in the event drugs which are easy to administer, such as oral medications, are available. If a product is approved, but does not achieve an adequate level of acceptance by physicians, patients and healthcare payors, we may not generate sufficient revenues from such product and we may not become or remain profitable. For example, several new antivirals have been approved for the treatment of the Hepatitis C infection since we commenced clinical development of RG-101. Such increased competition may decrease any future potential revenue for RG-101 due to increasing pressure for lower pricing and higher discounts in the commercialization of our product.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenues. *

We currently do not have an organization for the sales, marketing and distribution of pharmaceutical products and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. For example, in order to commercialize RG-101 or to exercise our co-promotion rights with Sanofi with respect to our miR-21 and miR-221/222 programs, we would need to build our sales, marketing, managerial and other non-technical capabilities in order to effectively carry out sales or co-promotion activities with respect to any approved products that are developed through these programs. With respect to certain of our current programs that are the subject of existing strategic alliances, such as the metabolic and oncology programs with AstraZeneca, we intend to rely completely on our alliance partner for sales and marketing. In addition, we intend to enter into strategic alliances with third parties to commercialize other product candidates, including in markets outside of the United States or for other large markets that are beyond our resources. Although we intend to establish a sales organization if we are able to obtain approval to market any product candidates for niche markets in the United States, we will also consider the option to enter into strategic alliances for future product candidates in the United States if commercialization requirements exceed our available resources. This will reduce the revenue generated from the sales of these products.

Our current and future strategic alliance partners, if any, may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective alliances to enable the sale of our product candidates to healthcare professionals and in geographical regions, including the United States, that will not be covered by our own marketing and sales force, or if our potential future

strategic alliance partners do not successfully commercialize the product candidates, our ability to generate revenues from product sales will be adversely affected.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

If we obtain approval to commercialize any approved products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

Under our strategic alliance agreements with Sanofi and AstraZeneca, they will be responsible for the commercialization of future product candidates, if any, from their respective programs, as applicable. If any other product candidates that we may develop are approved for commercialization, we may also enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Coverage and adequate reimbursement may not be available for our product candidates, which could make it difficult for us to sell products profitably.

Market acceptance and sales of any product candidates that we develop will depend on coverage and reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third party payors, such as private health insurers, government payors and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that coverage and adequate reimbursement will be available for any future product candidates. Also, inadequate reimbursement amounts may reduce the demand for, or the price of, our future products. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialize product candidates that we develop.

In addition, we cannot be certain if and when we will obtain formulary approval to allow us to sell any products that we may develop and commercialize into our target markets. Obtaining formulary approval from hospitals and from payors can be an expensive and time consuming process. Failure to obtain timely formulary approval will limit our commercial success.

There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell products profitably. These legislative and/or regulatory changes may negatively impact the reimbursement for drug products, following approval. The availability of numerous generic treatments may also substantially reduce the likelihood of reimbursement for our future products. The potential application of user fees to generic drug products may expedite the approval of additional generic drug treatments. We expect to experience pricing pressures in connection with the sale of any products that we develop, due to the trend toward managed healthcare, the

increasing influence of health maintenance organizations and additional legislative changes. If we fail to successfully secure and maintain reimbursement coverage for our future products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our future products and our business will be harmed.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the U.S. and generally tend to be priced significantly lower.

RISKS RELATED TO OUR BUSINESS OPERATIONS AND INDUSTRY

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are “at will” employees. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical companies for individuals with similar skill sets. In addition, failure to succeed in preclinical studies and clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

We may need to expand our organization and may experience difficulties in managing this growth, which could disrupt our operations.*

As of June 30, 2016, we had 96 full-time employees. As our company matures, we expect to expand our employee base to increase our managerial, scientific and operational, commercial, financial and other resources and to hire more consultants and contractors. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. Moreover, if our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct, but it is not always

possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Certain current and future relationships with customers and third party payors as well as certain of our business operations may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, further subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The healthcare laws and regulations that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to the federal government, including Medicare or Medicaid, that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, which imposes certain requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians, and further requires applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members; 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 items or services reimbursed by any third party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that 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 certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, possible exclusion from Medicare, Medicaid and other government healthcare programs, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Recent and future healthcare legislation may further impact our business operations.

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

By way of example, in March 2010, the PPACA was signed into law, intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the health industry and impose additional health policy reforms. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a new Medicare Part D coverage gap discount program, in which manufacturers 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 a manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors.

There have been judicial and Congressional challenges and amendments to certain aspects of the PPACA, and we expect there will be additional challenges and amendments to the PPACA in the future. Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. Certain oligonucleotide therapeutics have shown injection site reactions and pro-inflammatory effects and may also lead to impairment of kidney or liver function. There is a risk that our current and future product candidates may induce similar adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We maintain product liability insurance relating to the use of our therapeutics in clinical trials. However, such insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Cyber security risks and the failure to maintain the confidentiality, integrity, and availability of our computer hardware, software, and Internet applications and related tools and functions could result in damage to our reputation and/or subject us to costs, fines or lawsuits.

Our business requires manipulating, analyzing and storing large amounts of data. In addition, we rely on a global enterprise software system to operate and manage our business. We also maintain personally identifiable information about our employees. Our business therefore depends on the continuous, effective, reliable, and secure operation of our computer hardware, software, networks, Internet servers, and related infrastructure. To the extent that our hardware or software malfunctions or access to our data by internal research personnel is interrupted, our business could suffer. The integrity and protection of our employee and company data is critical to our business and employees have a high expectation that we will adequately protect their personal information. The regulatory environment governing information, security and privacy laws is increasingly demanding and continues to evolve. Maintaining compliance with applicable security and privacy regulations may increase our operating costs. Although our computer and communications hardware is protected through physical and software safeguards, it is still vulnerable to fire, storm, flood, power loss, earthquakes, telecommunications failures, physical or software break-ins, software viruses, and similar events. These events could lead to the unauthorized access, disclosure and use of non-public information. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world. As a result, we may not be able to address these techniques proactively or implement adequate preventative measures. If our computer systems are compromised, we could be subject to fines, damages, litigation and enforcement actions, and we could lose trade secrets, the occurrence of which could harm our business. In addition, any sustained disruption in internet access provided by other companies could harm our business.

Business interruptions could delay us in the process of developing our future products.

Our headquarters are located in San Diego County. We are vulnerable to natural disasters such as earthquakes and wild fires, as well as other events that could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

RISKS RELATED TO OUR COMMON STOCK

The market price of our common stock may be highly volatile.*

Since shares of our common stock were sold in our initial public offering in October 2012 at a price of \$4.00 per share, our closing stock price as reported on The NASDAQ Global Market has ranged from \$2.44 to \$22.08, through July 29, 2016. The trading price of our common stock is likely to continue to be volatile.

Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in preclinical studies or clinical trials;
- inability to obtain additional funding;
- any delay in filing an IND or NDA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA’s review of that IND or NDA;
- failure to maintain our existing strategic alliances or enter into new alliances;
- failure of our strategic alliance partners to elect to develop and commercialize product candidates under our alliance agreements or the termination of any programs under our alliance agreements;
- failure by us or our licensors and strategic alliance partners to prosecute, maintain or enforce our intellectual property rights;
- failure to successfully develop and commercialize our product candidates;
- changes in laws or regulations applicable to our preclinical and clinical development activities, product candidates or future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic alliance partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, companies trading in the stock market in general, and The NASDAQ Global Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Our principal stockholders and management beneficially own a majority of our stock and will be able to exert significant control over matters subject to stockholder approval.*

As of July 29, 2016, our executive officers, directors, 5% stockholders and their affiliates beneficially owned a majority of our outstanding voting stock. Therefore, these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We are an “emerging growth company,” and the reduced reporting requirements applicable to emerging growth companies could make our common stock less attractive to investors.

We are currently an “emerging growth company,” as defined in the JOBS Act. As an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not “emerging growth companies,” including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company through December 31, 2017, although we may lose that status sooner. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

The requirements of being a publicly traded company may strain our resources and divert management’s attention.

As a publicly traded company, we have incurred, and will continue to incur, significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and The NASDAQ Global Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as “say on pay” and proxy access. As an “emerging growth company” we are permitted to implement many of these requirements over a longer period and up to five years from the pricing of our initial public offering. We have taken advantage of this new legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are or may become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of our securities are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act. Pursuant to our registration statements on Form S-3 which became effective in April 2014 and in April 2015, up to 7,190,422 shares held by certain of our stockholders remain available for resale thereunder. We may file additional registration statements in the future to provide for the further sale of shares of common stock by our stockholders. Any further sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell

common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. Pursuant to our registration statement on Form S-3 that became effective on April 16, 2014, we may sell up to \$18.2 million of common stock or warrants from time to time in one or more public offerings. On April 8, 2015, we filed a shelf registration statement on Form S-3, which we subsequently amended on February 23, 2016 and which is currently effective. Under the shelf registration statement, as amended, we may offer to sell from time to time in one or more offerings shares of our common stock in an aggregate amount of up to \$150 million. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. In addition, we may file additional registration statements in the future to provide for the further sale of shares of common stock by us or by selling stockholders.

Pursuant to our 2012 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2012 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the preceding calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. In addition, we may grant or provide for the grant of rights to purchase shares of our common stock pursuant to the ESPP. The number of shares of our common stock reserved for issuance under the ESPP will automatically increase on January 1 of each calendar year by the lesser of 1% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year and 500,000 shares, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2012 Plan and ESPP each year. Pursuant to our Inducement Plan, our management is authorized to grant stock options exercisable for up to an aggregate of 1,000,000 shares of our common stock to new employees as inducements material to such new employees entering into employment with us. The number of shares which may be granted under the Inducement Plan may be increased in the future by our board of directors.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We triggered an "ownership change" limitation at the completion of our initial public offering in October 2012 and again in July 2015. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock. *

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, our ability to pay cash dividends is currently prohibited by the terms of our secured debt, and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock.

Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

- authorizing the issuance of “blank check” preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders;
- establishing the state of Delaware as the sole forum for certain legal actions against the Company, its officers and directors; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change in control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Recent Sales of Unregistered Securities

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

For a list of exhibits filed with this quarterly report on Form 10-Q, refer to the Exhibit Index immediately following the signature page to this quarterly report.

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.

Date: August 2, 2016

Regulus Therapeutics Inc.
By: /s/ Paul C. Grint
Paul C. Grint, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: August 2, 2016

By: /s/ Joseph P. Hagan
Joseph P. Hagan
Chief Operating Officer
(Principal Financial and Accounting Officer)

EXHIBIT INDEX

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant.
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on June 8, 2016).
4.1	Reference is made to Exhibits 3.1 and 3.2.
4.2	Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012).
10.1	Loan and Security Agreement, dated June 17, 2016, among the Registrant and Oxford Finance LLC.
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1*	Certification of the Principal Executive Officer and the Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
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 Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

* These certifications are being furnished solely to accompany this quarterly report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

**AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION OF
REGULUS THERAPEUTICS INC.**

Regulus Therapeutics Inc., a corporation organized and existing under the laws of the State of Delaware, hereby certifies as follows:

FIRST : The name of this corporation is Regulus Therapeutics Inc.

SECOND : The date on which the corporation's Certificate of Incorporation was originally filed with the Secretary of State of the State of Delaware is January 2, 2009.

THIRD : The Certificate of Incorporation of said corporation shall be amended and restated to read in full as follows:

I.

The name of this corporation is Regulus Therapeutics Inc. (the "*Company*").

II.

The address of the registered office of the Company in the State of Delaware is 1209 Orange Street, City of Wilmington, County of New Castle, Delaware, 19801 and the name of the registered agent of the Company in the State of Delaware at such address is The Corporation Trust Company.

III.

The purpose of the Company is to engage in any lawful act or activity for which a corporation may be organized under the Delaware General Corporation Law (the "*DGCL*").

IV.

A. The Company is authorized to issue two classes of stock to be designated, respectively, "Common Stock" and "Preferred Stock." The total number of shares which the Company is authorized to issue is 210,000,000 shares. 200,000,000 shares shall be Common Stock, each having a par value of \$0.001. 10,000,000 shares shall be Preferred Stock, each having a par value of \$0.001.

B. The Preferred Stock may be issued from time to time in one or more series. The Board of Directors of the Company (the "*Board of Directors*") is hereby expressly authorized to provide for the issue of any or all of the unissued and undesignated shares of the Preferred Stock in one or more series, and to fix the number of shares and to determine or alter for each such series, such voting powers, full or limited, or no voting powers, and such designation, preferences, and relative, participating, optional, or other rights and such qualifications, limitations, or restrictions thereof, as shall be stated and expressed in the resolution or resolutions adopted by the Board of Directors providing for the issuance of such shares and as may be permitted by the DGCL. The Board of Directors is also expressly authorized to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of such series then outstanding. In case the number of shares of any series shall be decreased in accordance with the foregoing sentence, the shares constituting such decrease shall resume the status that they had prior to the adoption of the resolution originally fixing the number of shares of such series. The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the voting power of the stock of the Company entitled to vote thereon, without a separate vote of the holders of the Preferred Stock, or of any series thereof, unless a vote of any such holders is required pursuant to the terms of any certificate of designation filed with respect to any series of Preferred Stock.

C. Each outstanding share of Common Stock shall entitle the holder thereof to one vote on each matter properly submitted to the stockholders of the Company for their vote; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Amended and Restated Certificate of Incorporation (this "*Certificate of Incorporation*") (including any certificate of designation filed with respect to any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such

affected series of Preferred Stock are entitled, either separately or together as a class with the holders of one or more other series of Preferred Stock, to vote thereon by law or pursuant to this Certificate of Incorporation (including any certificate of designation filed with respect to any series of Preferred Stock).

V.

For the management of the business and for the conduct of the affairs of the Company, and in further definition, limitation and regulation of the powers of the Company, of its directors and of its stockholders or any class thereof, as the case may be, it is further provided that:

A. The management of the business and the conduct of the affairs of the Company shall be vested in its Board of Directors. The number of directors that shall constitute the Board of Directors shall be fixed exclusively by resolutions adopted by a majority of the authorized number of directors constituting the Board of Directors.

B. Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, the directors shall be elected at each annual meeting of stockholders to hold office until the next annual meeting. Each director shall hold office either until the expiration of the term for which elected or appointed and until a successor has been elected and qualified, or until such director's earlier death, resignation or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

C. Subject to the rights of any series of Preferred Stock that may be designated from time to time to elect additional directors under specified circumstances, and subject to any limitation imposed by law, any individual director or directors may be removed with or without cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the Company entitled to vote generally at an election of directors, voting together as a single class.

D. Subject to the rights of the holders of any series of Preferred Stock that may be designated from time to time, any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors, shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by the stockholders, except as otherwise provided by law, be filled only by the affirmative vote of a majority of the directors then in office, even though less than a quorum of the Board of Directors, and not by the stockholders. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified.

E. Subject to the rights of the holders of any series of Preferred Stock that may be designated from time to time, the Board of Directors is expressly empowered to adopt, amend or repeal the Amended and Restated Bylaws of the Company (the "*Bylaws*"). Any adoption, amendment or repeal of the Bylaws by the Board of Directors shall require the approval of a majority of the authorized number of directors. The stockholders shall also have power to adopt, amend or repeal the Bylaws, subject to any restrictions which may be set forth in this Certificate of Incorporation (including any certificate of designation that may be filed from time to time); provided, however, that, in addition to any vote of the holders of any class or series of stock of the Company required by law or by this Certificate of Incorporation, such action by stockholders shall require the affirmative vote of the holders of at least $66 \frac{2}{3}$ % of the voting power of all of the then-outstanding shares of the capital stock of the Company entitled to vote generally at an election of directors, voting together as a single class.

F. The directors of the Company need not be elected by written ballot unless the Bylaws so provide.

G. No action shall be taken by the stockholders of the Company except at an annual or special meeting of stockholders called in accordance with the Bylaws. No action shall be taken by the stockholders of the Company by written consent or electronic transmission.

H. Advance notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of the stockholders of the Company shall be given in the manner provided in the Bylaws.

VI.

A. The liability of a director of the Company for monetary damages shall be eliminated to the fullest extent under applicable law. If the DGCL is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Company shall be eliminated to the fullest extent permitted by the DGCL, as so amended.

B. Any repeal or modification of this Article VI shall be prospective and shall not affect the rights under this Article VI in effect at the time of the alleged occurrence of any act or omission to act giving rise to liability or indemnification.

VII.

A. The Company reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute, except as provided in Section B of this Article VII, and all rights conferred upon the stockholders herein are granted subject to this reservation.

B. Notwithstanding any other provisions of this Certificate of Incorporation or any provision of law which might otherwise permit a lesser vote or no vote, but in addition to any affirmative vote of the holders of any particular class or series of the Company required by law or by this Certificate of Incorporation or any certificate of designation filed with respect to a series of Preferred Stock that may be designated from time to time, subject to the rights of the holders of any series of Preferred Stock, the affirmative vote of the holders of at least 66 ²/₃ % of the voting power of all of the then-outstanding shares of capital stock of the Company entitled to vote generally at an election of directors, voting together as a single class, shall be required to alter, amend or repeal Articles V, VI or VII of this Certificate of Incorporation.

* * * *

F O U R T H : This Amended and Restated Certificate of Incorporation has been duly adopted and approved by the Board of Directors.

F I F T H : This Amended and Restated Certificate of Incorporation has been duly adopted and approved by the stockholders in accordance with sections 211, 242 and 245 of the DGCL.

I N W I T N E S S W H E R E O F , Regulus Therapeutics Inc. has caused this Amended and Restated Certificate of Incorporation to be signed by its President and Chief Executive Officer this 2nd day of June, 2016.

R E G U L U S T H E R A P E U T I C S I N C .

P A U L C . G R I N T , M . D .

President and Chief Executive Officer

LOAN AND SECURITY AGREEMENT

THIS LOAN AND SECURITY AGREEMENT (as the same may from time to time be amended, modified, supplemented or restated, this “**Agreement**”) dated as of June 17, 2016 (the “**Effective Date**”) among OXFORD FINANCE LLC, a Delaware limited liability company with an office located at 133 North Fairfax Street, Alexandria, Virginia 22314 (“**Oxford**”), as collateral agent (in such capacity, “**Collateral Agent**”), the Lenders listed on Schedule 1.1 hereof or otherwise a party hereto from time to time including Oxford in its capacity as a Lender (each a “**Lender**” and collectively, the “**Lenders**”), and REGULUS THERAPEUTICS INC., a Delaware corporation with offices located at 10614 Science Center Dr., San Diego, California 92121 (“**Borrower**”), provides the terms on which the Lenders shall lend to Borrower and Borrower shall repay the Lenders. The parties agree as follows:

1. ACCOUNTING AND OTHER TERMS

1.1 Accounting terms not defined in this Agreement shall be construed in accordance with GAAP. Calculations and determinations must be made in accordance with GAAP. Capitalized terms not otherwise defined in this Agreement shall have the meanings set forth in Section 13. All other terms contained in this Agreement, unless otherwise indicated, shall have the meaning provided by the Code to the extent such terms are defined therein. All references to “**Dollars**” or “**\$**” are United States Dollars, unless otherwise noted.

2. LOANS AND TERMS OF PAYMENT

2.1 Promise to Pay. Borrower hereby unconditionally promises to pay each Lender, the outstanding principal amount of all Term Loans advanced to Borrower by such Lender and accrued and unpaid interest thereon and any other amounts due hereunder as and when due in accordance with this Agreement.

2.2 Term Loans.

(a) Availability.

(i) Subject to the terms and conditions of this Agreement, the Lenders agree, severally and not jointly, to make term loans to Borrower on or after the Effective Date, and on or prior to June 22, 2016, in an aggregate amount of Twenty Million Dollars (\$20,000,000.00) according to each Lender’s Term A Loan Commitment as set forth on Schedule 1.1 hereto (such term loans are hereinafter referred to singly as a “**Term A Loan**”, and collectively as the “**Term A Loans**”). After repayment, no Term A Loan may be re-borrowed.

(ii) Subject to the terms and conditions of this Agreement, the Lenders agree, severally and not jointly, during the Second Draw Period, to make term loans to Borrower in an aggregate amount up to Ten Million Dollars (\$10,000,000.00) according to each Lender’s Term B Loan Commitment as set forth on Schedule 1.1 hereto (such term loans are hereinafter referred to singly as a “**Term B Loan**”, and collectively as the “**Term B Loans**”; each Term A Loan or Term B Loan is hereinafter referred to singly as a “**Term Loan**” and the Term A Loans and the Term B Loans are hereinafter referred to collectively as the “**Term Loans**”). After repayment, no Term B Loan may be re-borrowed.

(b) Repayment. Borrower shall make monthly payments of interest only commencing on the first (1st) Payment Date following the Funding Date of each Term Loan, and continuing on the Payment Date of each successive month thereafter through and including the Payment Date immediately preceding the Amortization Date. Borrower agrees to pay, on the Funding Date of each Term Loan, any initial partial monthly interest payment otherwise due for the period between the Funding Date of such Term Loan and the last day of the calendar month during which the Funding Date occurs. Commencing on the Amortization Date, and continuing on the Payment Date of each month thereafter, Borrower shall make consecutive equal monthly payments of principal, together with applicable interest, in arrears, to each Lender, as calculated by Collateral Agent (which calculations shall be deemed correct absent manifest error) based upon: (1) the amount of such Lender’s Term Loan, (2) the effective rate of interest, as determined in Section 2.3(a), and (3) a repayment schedule equal to twenty-four (24) months with respect to the Term Loans. All unpaid principal and accrued and unpaid interest with respect to each Term Loan is due and payable in full on the Maturity Date. Each Term Loan may only be prepaid in accordance with Sections 2.2(c) and 2.2(d).

(c) Mandatory Prepayments. If the Term Loans are accelerated following the occurrence of an Event of Default, Borrower shall immediately pay to Lenders, payable to each Lender in accordance with its respective Pro Rata Share, an amount equal to the sum of: (i) all outstanding principal of the Term Loans plus accrued and unpaid interest thereon through the

prepayment date, (ii) the Final Payment, (iii) the Prepayment Fee, plus (iv) all other Obligations that are due and payable, including Lenders' Expenses and interest at the Default Rate with respect to any past due amounts. Notwithstanding (but without duplication with) the foregoing, on the Maturity Date, if the Final Payment had not previously been paid in full in connection with the prepayment of the Term Loans in full, Borrower shall pay to Collateral Agent, for payment to each Lender in accordance with its respective Pro Rata Share, the Final Payment in respect of the Term Loan(s).

(d) Permitted Prepayment of Term Loans. Borrower shall have the option to prepay all, but not less than all, of the Term Loans advanced by the Lenders under this Agreement, provided Borrower (i) provides written notice to Collateral Agent of its election to prepay the Term Loans at least ten (10) days prior to such prepayment, and (ii) pays to the Lenders on the date of such prepayment, payable to each Lender in accordance with its respective Pro Rata Share, an amount equal to the sum of (A) all outstanding principal of the Term Loans plus accrued and unpaid interest thereon through the prepayment date, (B) the Final Payment, (C) the Prepayment Fee, plus (D) all other Obligations that are due and payable, including Lenders' Expenses and interest at the Default Rate with respect to any past due amounts.

2.3 Payment of Interest on the Credit Extensions.

(a) Interest Rate. Subject to Section 2.3(b), the principal amount outstanding under the Term Loans shall accrue interest at a floating per annum rate equal to the Basic Rate, determined by Collateral Agent on the Funding Date of each Term Loan and then monthly thereafter, which interest shall be payable monthly in arrears in accordance with Sections 2.2(b) and 2.3(e). Interest shall accrue on each Term Loan commencing on, and including, the Funding Date of such Term Loan, and shall accrue on the principal amount outstanding under such Term Loan through and including the day on which such Term Loan is paid in full.

(b) Default Rate. Immediately upon the occurrence and during the continuance of an Event of Default, Obligations shall accrue interest at a floating per annum rate equal to the rate that is otherwise applicable thereto plus five percentage points (5.00%) (the "**Default Rate**"). Payment or acceptance of the increased interest rate provided in this Section 2.3(b) is not a permitted alternative to timely payment and shall not constitute a waiver of any Event of Default or otherwise prejudice or limit any rights or remedies of Collateral Agent.

(c) 360-Day Year. Interest shall be computed on the basis of a three hundred sixty (360) day year, and the actual number of days elapsed.

(d) Debit of Accounts. Collateral Agent and each Lender may debit (or ACH) any deposit accounts, maintained by Borrower or any of its Subsidiaries, including the Designated Deposit Account, for principal and interest payments or any other amounts Borrower owes the Lenders under the Loan Documents when due. Any such debits (or ACH activity) shall not constitute a set-off.

(e) Payments. Except as otherwise expressly provided herein, all payments by Borrower under the Loan Documents shall be made to the respective Lender to which such payments are owed, at such Lender's office in immediately available funds on the date specified herein. Unless otherwise provided, interest is payable monthly on the Payment Date of each month. Payments of principal and/or interest received after 12:00 noon Eastern time are considered received at the opening of business on the next Business Day. When a payment is due on a day that is not a Business Day, the payment is due the next Business Day and additional fees or interest, as applicable, shall continue to accrue until paid. All payments to be made by Borrower hereunder or under any other Loan Document, including payments of principal and interest, and all fees, expenses, indemnities and reimbursements, shall be made without set-off, recoupment or counterclaim, in lawful money of the United States and in immediately available funds.

2.4 Secured Promissory Notes. The Term Loans shall be evidenced by a Secured Promissory Note or Notes in the form attached as Exhibit D hereto (each a "**Secured Promissory Note**"), and shall be repayable as set forth in this Agreement. Borrower irrevocably authorizes each Lender to make or cause to be made, on or about the Funding Date of any Term Loan or at the time of receipt of any payment of principal on such Lender's Secured Promissory Note, an appropriate notation on such Lender's Secured Promissory Note Record reflecting the making of such Term Loan or (as the case may be) the receipt of such payment. The outstanding amount of each Term Loan set forth on such Lender's Secured Promissory Note Record shall be prima facie evidence of the principal amount thereof owing and unpaid to such Lender, but the failure to record, or any error in so recording, any such amount on such Lender's Secured Promissory Note Record shall not limit or otherwise affect the obligations of Borrower under any Secured Promissory Note or any other Loan Document to make payments of principal or interest on any Secured Promissory Note when due. Upon receipt of an affidavit of an officer of a Lender as to the loss, theft, destruction, or mutilation of its Secured Promissory Note, with an appropriate indemnity, Borrower shall issue, in lieu thereof, a replacement Secured Promissory Note in the same principal amount thereof and of like tenor.

2.5 Fees. Borrower shall pay to Collateral Agent:

- (a) **Good Faith Deposit.** An amount of Thirty Thousand Dollars (\$30,000.00), which amount has been received by Collateral Agent as a good faith deposit from Borrower on or about June 6, 2016 and shall be applied towards Lenders' Expenses incurred through the Effective Date payable pursuant to Section 2.5(e) hereof, and the balance left over, if any, shall be applied towards the facility fee due pursuant to Section 2.5(b) hereof. For the purposes of clarity, Borrower shall be responsible for all Lender's Expenses payable pursuant to Section 2.5(e) hereof and the facility fee due pursuant to Section 2.5(b) hereof;
- (b) **Facility Fee.** A fully earned, non-refundable facility fee of One Hundred Fifty Thousand Dollars (\$150,000.00) to be shared between the Lenders pursuant to their respective Commitment Percentages payable on the Effective Date;
- (c) **Final Payment.** The Final Payment, when due hereunder, to be shared between the Lenders in accordance with their respective Pro Rata Shares;
- (d) **Prepayment Fee.** The Prepayment Fee, when due hereunder, to be shared between the Lenders in accordance with their respective Pro Rata Shares; and
- (e) **Lenders' Expenses.** All Lenders' Expenses (including reasonable attorneys' fees and expenses for documentation and negotiation of this Agreement) incurred through and after the Effective Date, when due.

2.6 Withholding. Payments received by the Lenders from Borrower hereunder will be made free and clear of and without deduction for any and all present or future taxes, levies, imposts, duties, deductions, withholdings, assessments, fees or other charges imposed by any governmental authority (including any interest, additions to tax or penalties applicable thereto). Specifically, however, if at any time any Governmental Authority, applicable law, regulation or international agreement requires Borrower to make any withholding or deduction from any such payment or other sum payable hereunder to the Lenders, Borrower hereby covenants and agrees that the amount due from Borrower with respect to such payment or other sum payable hereunder will be increased to the extent necessary to ensure that, after the making of such required withholding or deduction, each Lender receives a net sum equal to the sum which it would have received had no withholding or deduction been required and Borrower shall pay the full amount withheld or deducted to the relevant Governmental Authority. Borrower will, upon request, furnish the Lenders with proof reasonably satisfactory to the Lenders indicating that Borrower has made such withholding payment; provided, however, that Borrower need not make any withholding payment if the amount or validity of such withholding payment is contested in good faith by appropriate and timely proceedings and as to which payment in full is bonded or reserved against by Borrower. The agreements and obligations of Borrower contained in this Section 2.6 shall survive the termination of this Agreement.

3. CONDITIONS OF LOANS

3.1 Conditions Precedent to Initial Credit Extension. Each Lender's obligation to make a Term A Loan is subject to the condition precedent that Collateral Agent and each Lender shall consent to or shall have received, in form and substance satisfactory to Collateral Agent and each Lender, such documents, and completion of such other matters, as Collateral Agent and each Lender may reasonably deem necessary or appropriate, including, without limitation:

- (a) original Loan Documents, each duly executed by Borrower and each Subsidiary, as applicable;
 - (b) duly executed original Control Agreements with respect to any Collateral Accounts maintained by Borrower or any of its Subsidiaries;
 - (c) duly executed original Secured Promissory Notes in favor of each Lender according to its Term A Loan Commitment Percentage;
 - (d) the Operating Documents and good standing certificates of Borrower and its Subsidiaries certified by the Secretary of State (or equivalent agency) of Borrower's and such Subsidiaries' jurisdiction of organization or formation and each jurisdiction in which Borrower and each Subsidiary is qualified to conduct business, each as of a date no earlier than thirty (30) days prior to the Funding Date of the Term A Loans ;
 - (e) a completed Perfection Certificate for Borrower and each of its Subsidiaries;
 - (f) the Annual Projections, for the current calendar year;
-

(g) duly executed original officer's certificate for Borrower and each Subsidiary that is a party to the Loan Documents, in a form acceptable to Collateral Agent and the Lenders;

(h) certified copies, dated as of date no earlier than thirty (30) days prior to the Funding Date of the Term A Loans, of financing statement searches, as Collateral Agent shall request, accompanied by written evidence (including any UCC termination statements) that the Liens indicated in any such financing statements either constitute Permitted Liens or have been or, in connection with the initial Credit Extension, will be terminated or released;

(i) a landlord's consent executed in favor of Collateral Agent in respect of all of Borrower's and each Subsidiaries' leased locations;

(j) a bailee waiver executed in favor of Collateral Agent in respect of each third party bailee where Borrower or any Subsidiary maintains Collateral having a book value in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00); provided that this condition shall not apply to active pharmaceutical ingredient, other raw materials, or concomitant medications intended for use in the Borrower's preclinical or clinical trials;

(k) a duly executed legal opinion of counsel to Borrower dated as of the Funding Date of the Term A Loans;

(l) evidence satisfactory to Collateral Agent and the Lenders that the insurance policies required by Section 6.5 hereof are in full force and effect, together with appropriate evidence showing loss payable and/or additional insured clauses or endorsements in favor of Collateral Agent, for the ratable benefit of the Lenders; and

(m) payment of the fees and Lenders' Expenses then due as specified in Section 2.5 hereof.

3.2 Conditions Precedent to all Credit Extensions. The obligation of each Lender to make each Credit Extension, including the initial Credit Extension, is subject to the following conditions precedent:

(a) receipt by Collateral Agent of an executed Disbursement Letter in the form of Exhibit B attached hereto;

(b) the representations and warranties in Section 5 hereof shall be true, accurate and complete in all material respects on the date of the Disbursement Letter and on the Funding Date of each Credit Extension; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true, accurate and complete in all material respects as of such date, and no Event of Default shall have occurred and be continuing or result from the Credit Extension. Each Credit Extension is Borrower's representation and warranty on that date that the representations and warranties in Section 5 hereof are true, accurate and complete in all material respects; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true, accurate and complete in all material respects as of such date;

(c) in such Lender's sole but reasonable discretion, there has not been any Material Adverse Change or any material adverse deviation by Borrower from the Annual Projections of Borrower presented to and accepted by Collateral Agent and each Lender;

(d) to the extent not delivered at the Effective Date, duly executed original Secured Promissory Notes, in number, form and content acceptable to each Lender, and in favor of each Lender according to its Commitment Percentage, with respect to each Credit Extension made by such Lender after the Effective Date; and

(e) payment of the fees and Lenders' Expenses then due as specified in Section 2.5 hereof.

3.3 Covenant to Deliver. Borrower agrees to deliver to Collateral Agent and the Lenders each item required to be delivered to Collateral Agent under this Agreement as a condition precedent to any Credit Extension. Borrower expressly agrees that a Credit Extension made prior to the receipt by Collateral Agent or any Lender of any such item shall not constitute a waiver by Collateral Agent or any Lender of Borrower's obligation to deliver such item, and any such Credit Extension in the absence of a required item shall be made in each Lender's sole discretion.

3.4 Procedures for Borrowing. Subject to the prior satisfaction of all other applicable conditions to the making of a Term Loan set forth in this Agreement, to obtain a Term Loan, Borrower shall notify the Lenders (which notice shall be irrevocable) by electronic mail, facsimile, or telephone by 12:00 noon Eastern time three (3) Business Days prior to the date the

Term Loan is to be made. Together with any such electronic, facsimile or telephonic notification, Borrower shall deliver to the Lenders by electronic mail or facsimile a completed Disbursement Letter executed by a Responsible Officer or his or her designee. The Lenders may rely on any telephone notice given by a person whom a Lender reasonably believes is a Responsible Officer or designee. On the Funding Date, each Lender shall credit and/or transfer (as applicable) to the Designated Deposit Account, an amount equal to its Term Loan Commitment.

4. CREATION OF SECURITY INTEREST

4.1 Grant of Security Interest. Borrower hereby grants Collateral Agent, for the ratable benefit of the Lenders, to secure the payment and performance in full of all of the Obligations, a continuing security interest in, and pledges to Collateral Agent, for the ratable benefit of the Lenders, the Collateral, wherever located, whether now owned or hereafter acquired or arising, and all proceeds and products thereof. Borrower represents, warrants, and covenants that the security interest granted herein is and shall at all times continue to be a first priority perfected security interest in the Collateral, subject only to Permitted Liens that are permitted by the terms of this Agreement to have priority to Collateral Agent's Lien. If Borrower shall acquire a commercial tort claim (as defined in the Code), Borrower, shall promptly notify Collateral Agent in a writing signed by Borrower, as the case may be, of the general details thereof (and further details as may be required by Collateral Agent) and grant to Collateral Agent, for the ratable benefit of the Lenders, in such writing a security interest therein and in the proceeds thereof, all upon the terms of this Agreement, with such writing to be in form and substance reasonably satisfactory to Collateral Agent.

If this Agreement is terminated, Collateral Agent's Lien in the Collateral shall continue until the Obligations (other than inchoate indemnity obligations) are repaid in full in cash. Upon payment in full in cash of the Obligations (other than inchoate indemnity obligations) and at such time as the Lenders' obligation to make Credit Extensions has terminated, Collateral Agent shall, at the sole cost and expense of Borrower, release its Liens in the Collateral and all rights therein shall revert to Borrower.

4.2 Authorization to File Financing Statements. Borrower hereby authorizes Collateral Agent to file financing statements or take any other action required to perfect Collateral Agent's security interests in the Collateral, without notice to Borrower, with all appropriate jurisdictions to perfect or protect Collateral Agent's interest or rights under the Loan Documents, including a notice that any disposition of the Collateral, except to the extent permitted by the terms of this Agreement, by Borrower, or any other Person, shall be deemed to violate the rights of Collateral Agent under the Code.

5. REPRESENTATIONS AND WARRANTIES

Borrower represents and warrants to Collateral Agent and the Lenders as follows:

5.1 Due Organization, Authorization: Power and Authority. Borrower and each of its Subsidiaries is duly existing and in good standing as a Registered Organization in its jurisdictions of organization or formation and Borrower and each of its Subsidiaries is qualified and licensed to do business and is in good standing in any jurisdiction in which the conduct of its businesses or its ownership of property requires that it be qualified except where the failure to do so could not reasonably be expected to have a Material Adverse Change. In connection with this Agreement, Borrower and each of its Subsidiaries has delivered to Collateral Agent a completed perfection certificate signed by an officer of Borrower or such Subsidiary (each a "**Perfection Certificate**" and collectively, the "**Perfection Certificates**"). Borrower represents and warrants that (a) Borrower and each of its Subsidiaries' exact legal name is that which is indicated on its respective Perfection Certificate and on the signature page of each Loan Document to which it is a party; (b) Borrower and each of its Subsidiaries is an organization of the type and is organized in the jurisdiction set forth on its respective Perfection Certificate; (c) each Perfection Certificate accurately sets forth each of Borrower's and its Subsidiaries' organizational identification number or accurately states that Borrower or such Subsidiary has none; (d) each Perfection Certificate accurately sets forth Borrower's and each of its Subsidiaries' place of business, or, if more than one, its chief executive office as well as Borrower's and each of its Subsidiaries' mailing address (if different than its chief executive office); (e) Borrower and each of its Subsidiaries (and each of its respective predecessors) have not, in the past five (5) years, changed its jurisdiction of organization, organizational structure or type, or any organizational number assigned by its jurisdiction; and (f) all other information set forth on the Perfection Certificates pertaining to Borrower and each of its Subsidiaries, is accurate and complete (it being understood and agreed that Borrower and each of its Subsidiaries may from time to time update certain information in the Perfection Certificates (including the information set forth in clause (d) above) after the Effective Date to the extent permitted by one or more specific provisions in this Agreement); such updated Perfection Certificates subject to the review and approval of Collateral Agent. If Borrower or any of its Subsidiaries is not now a Registered Organization but later becomes one, Borrower shall notify Collateral Agent of such occurrence and provide Collateral Agent with such Person's organizational identification number within five (5) Business Days of receiving such organizational identification number.

The execution, delivery and performance by Borrower and each of its Subsidiaries of the Loan Documents to which it is a party have been duly authorized, and do not (i) conflict with any of Borrower's or such Subsidiaries' organizational documents,

including its respective Operating Documents, (ii) contravene, conflict with, constitute a default under or violate any material Requirement of Law applicable thereto, (iii) contravene, conflict or violate any applicable order, writ, judgment, injunction, decree, determination or award of any Governmental Authority by which Borrower or such Subsidiary, or any of their property or assets may be bound or affected, (iv) require any action by, filing, registration, or qualification with, or Governmental Approval from, any Governmental Authority (except such Governmental Approvals which have already been obtained and are in full force and effect) or are being obtained pursuant to Section 6.1(b), or (v) constitute an event of default under any material agreement by which Borrower or any of such Subsidiaries, or their respective properties, is bound. Neither Borrower nor any of its Subsidiaries is in default under any agreement to which it is a party or by which it or any of its assets is bound in which such default could reasonably be expected to have a Material Adverse Change.

5.2 Collateral.

(a) Borrower and each of its Subsidiaries have good title to, have rights in, and the power to transfer each item of the Collateral upon which it purports to grant a Lien under the Loan Documents, free and clear of any and all Liens except Permitted Liens, and neither Borrower nor any of its Subsidiaries have any Deposit Accounts, Securities Accounts, Commodity Accounts or other investment accounts other than the Collateral Accounts or the other investment accounts, if any, described in the Perfection Certificates delivered to Collateral Agent in connection herewith (as the same may be updated from time to time, provided that any such updates shall be in form and substance acceptable to Collateral Agent in its sole discretion) with respect of which Borrower or such Subsidiary has given Collateral Agent notice and taken such actions as are necessary to give Collateral Agent a perfected security interest therein. The Accounts are bona fide, existing obligations of the Account Debtors.

(b) On the Effective Date, and except as disclosed on the Perfection Certificate (as the same may be updated from time to time, provided that any such updates shall be in form and substance acceptable to Collateral Agent in its sole discretion) (i) the Collateral is not in the possession of any third party bailee (such as a warehouse), or (ii) no such third party bailee possesses components of the Collateral in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00); provided that, this representation and warranty shall not apply to active pharmaceutical ingredient, other raw materials, or concomitant medications intended for use in the Borrower's preclinical or clinical trials. None of the components of the Collateral (other than active pharmaceutical ingredient, other raw materials, or concomitant medications intended for use in the Borrower's preclinical or clinical trials) valued in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00) in the aggregate shall be maintained at a location other than as disclosed in the Perfection Certificates on the Effective Date or as permitted pursuant to Section 6.11.

(c) All Inventory is in all material respects of good and marketable quality, free from material defects.

(d) Borrower and each of its Subsidiaries is the sole owner of the Intellectual Property each respectively purports to own, free and clear of all Liens other than Permitted Liens. Except as noted on the Perfection Certificates or as notified to Collateral Agent pursuant to the last sentence of this Section 5.2(d), neither Borrower nor any of its Subsidiaries is a party to, nor is bound by, any material license or other material agreement with respect to which Borrower or such Subsidiary is the licensee that (i) prohibits or otherwise restricts Borrower or its Subsidiaries from granting a security interest in Borrower's or such Subsidiaries' interest in such material license or material agreement or any other property, except for customary anti-assignment provisions, or (ii) for which a default under or termination of could interfere with Collateral Agent's or any Lender's right to sell any Collateral. Borrower shall provide written notice to Collateral Agent and each Lender within ten (10) days of Borrower or any of its Subsidiaries entering into or becoming bound by any material license or material agreement with respect to which Borrower or any Subsidiary is the licensee (other than over-the-counter software that is commercially available to the public).

5.3 Litigation. Except as disclosed (i) on the Perfection Certificates, or (ii) in accordance with Section 6.9 hereof, there are no actions, suits, investigations, or proceedings pending or, to the knowledge of the Responsible Officers, threatened in writing by or against Borrower or any of its Subsidiaries involving more than Two Hundred Fifty Thousand Dollars (\$250,000.00).

5.4 No Material Deterioration in Financial Condition; Financial Statements. All consolidated financial statements for Borrower and its Subsidiaries, delivered to Collateral Agent fairly present, in conformity with GAAP, in all material respects the consolidated financial condition of Borrower and its Subsidiaries, and the consolidated results of operations of Borrower and its Subsidiaries as of the dates and for the periods presented. There has not been any material deterioration in the consolidated financial condition of Borrower and its Subsidiaries since the date of the most recent financial statements submitted to any Lender.

5.5 Solvency. Borrower and each of its Subsidiaries is Solvent.

5.6 Regulatory Compliance. Neither Borrower nor any of its Subsidiaries is an "investment company" or a company "controlled" by an "investment company" under the Investment Company Act of 1940, as amended. Neither Borrower nor any of its Subsidiaries is engaged as one of its important activities in extending credit for margin stock (under Regulations X, T and

U of the Federal Reserve Board of Governors). Borrower and each of its Subsidiaries has complied in all material respects with the Federal Fair Labor Standards Act. Neither Borrower nor any of its Subsidiaries is a “holding company” or an “affiliate” of a “holding company” or a “subsidiary company” of a “holding company” as each term is defined and used in the Public Utility Holding Company Act of 2005. Neither Borrower nor any of its Subsidiaries has violated any laws, ordinances or rules, the violation of which could reasonably be expected to have a Material Adverse Change. Neither Borrower’s nor any of its Subsidiaries’ properties or assets has been used by Borrower or such Subsidiary or, to Borrower’s knowledge, by previous Persons, in disposing, producing, storing, treating, or transporting any hazardous substance other than in material compliance with applicable laws. Borrower and each of its Subsidiaries has obtained all consents, approvals and authorizations of, made all declarations or filings with, and given all notices to, all Governmental Authorities that are necessary to continue their respective businesses as currently conducted.

None of Borrower, any of its Subsidiaries, or any of Borrower’s or its Subsidiaries’ Affiliates or any of their respective agents acting or benefiting in any capacity in connection with the transactions contemplated by this Agreement is (i) in violation of any Anti-Terrorism Law, (ii) engaging in or conspiring to engage in any transaction that evades or avoids, or has the purpose of evading or avoiding or attempts to violate, any of the prohibitions set forth in any Anti-Terrorism Law, or (iii) is a Blocked Person. None of Borrower, any of its Subsidiaries, or to the knowledge of Borrower and any of their Affiliates or agents, acting or benefiting in any capacity in connection with the transactions contemplated by this Agreement, (x) conducts any business or engages in making or receiving any contribution of funds, goods or services to or for the benefit of any Blocked Person, or (y) deals in, or otherwise engages in any transaction relating to, any property or interest in property blocked pursuant to Executive Order No. 13224, any similar executive order or other Anti-Terrorism Law.

5.7 Investments. Neither Borrower nor any of its Subsidiaries owns any stock, shares, partnership interests or other equity securities except for Permitted Investments.

5.8 Tax Returns and Payments; Pension Contributions. Borrower and each of its Subsidiaries has timely filed or have timely obtained extensions for filing all required tax returns and reports, and Borrower and each of its Subsidiaries, has timely paid all foreign, federal, state, and local taxes, assessments, deposits and contributions owed by Borrower and such Subsidiaries, in all jurisdictions in which Borrower or any such Subsidiary is subject to taxes, including the United States, unless such taxes are being contested in accordance with the following sentence. Borrower and each of its Subsidiaries, may defer payment of any contested taxes, provided that Borrower or such Subsidiary, (a) in good faith contests its obligation to pay the taxes by appropriate proceedings promptly and diligently instituted and conducted, (b) notifies Collateral Agent in writing of the commencement of, and any material development in, the proceedings, and (c) posts bonds or takes any other steps required to prevent the Governmental Authority levying such contested taxes from obtaining a Lien upon any of the Collateral that is other than a “ **Permitted Lien** .” Neither Borrower nor any of its Subsidiaries is aware of any claims or adjustments proposed for any of Borrower’s or such Subsidiaries’, prior tax years which could result in additional taxes becoming due and payable by Borrower or its Subsidiaries. Borrower and each of its Subsidiaries have paid all amounts necessary to fund all present pension, profit sharing and deferred compensation plans in accordance with their terms, and neither Borrower nor any of its Subsidiaries have, withdrawn from participation in, and have not permitted partial or complete termination of, or permitted the occurrence of any other event with respect to, any such plan which could reasonably be expected to result in any liability of Borrower or its Subsidiaries, including any liability to the Pension Benefit Guaranty Corporation or its successors or any other Governmental Authority.

5.9 Use of Proceeds. Borrower shall use the proceeds of the Credit Extensions solely as working capital and to fund its general business requirements in accordance with the provisions of this Agreement, and not for personal, family, household or agricultural purposes.

5.10 Full Disclosure. No written representation, warranty or other statement of Borrower or any of its Subsidiaries in any certificate or written statement given to Collateral Agent or any Lender, as of the date such representation, warranty, or other statement was made, taken together with all such written certificates and written statements given to Collateral Agent or any Lender, contains any untrue statement of a material fact or omits to state a material fact necessary to make the statements contained in the certificates or statements not misleading (it being recognized that the projections and forecasts provided by Borrower in good faith and based upon reasonable assumptions are not viewed as facts and that actual results during the period or periods covered by such projections and forecasts may differ from the projected or forecasted results).

5.11 Definition of “ Knowledge.” For purposes of the Loan Documents, whenever a representation or warranty is made to Borrower’s knowledge or awareness, to the “best of” Borrower’s knowledge, or with a similar qualification, knowledge or awareness means the actual knowledge, after reasonable investigation, of the Responsible Officers.

6. AFFIRMATIVE COVENANTS

Borrower shall, and shall cause each of its Subsidiaries to, do all of the following:

6.1 Government Compliance.

(a) Maintain its and all its Subsidiaries' legal existence and good standing in their respective jurisdictions of organization and maintain qualification in each jurisdiction in which the failure to so qualify could reasonably be expected to have a Material Adverse Change. Comply with all laws, ordinances and regulations to which Borrower or any of its Subsidiaries is subject, the noncompliance with which could reasonably be expected to have a Material Adverse Change.

(b) Obtain and keep in full force and effect, all of the material Governmental Approvals necessary for the performance by Borrower and its Subsidiaries of their respective businesses and obligations under the Loan Documents and the grant of a security interest to Collateral Agent for the ratable benefit of the Lenders, in all of the Collateral. Borrower shall promptly provide copies to Collateral Agent of any material Governmental Approvals obtained by Borrower or any of its Subsidiaries.

6.2 Financial Statements, Reports, Certificates.

(a) Deliver to each Lender:

(i) as soon as available, but no later than thirty (30) days after the last day of each month (including, for the avoidance of doubt, the last month of each fiscal quarter), a company prepared consolidated and consolidating balance sheet and income statement covering the consolidated operations of Borrower and its Subsidiaries for such month certified by a Responsible Officer and in a form reasonably acceptable to Collateral Agent;

(ii) as soon as available, but no later than forty-five (45) days after the last day of each fiscal quarter, a company prepared consolidated and consolidating statement of cash flows covering the consolidated operations of Borrower and its Subsidiaries for such quarter certified by a Responsible Officer and in a form reasonably acceptable to Collateral Agent;

(iii) as soon as available, but no later than one hundred twenty (120) days after the last day of Borrower's fiscal year or within five (5) days of filing with the SEC, audited consolidated financial statements prepared under GAAP, consistently applied, together with an unqualified opinion on the financial statements from an independent certified public accounting firm acceptable to Collateral Agent in its reasonable discretion;

(iv) as soon as available after approval thereof by Borrower's Board of Directors, but no later than forty-five (45) days after the last day of each of Borrower's fiscal years, Borrower's annual financial projections for the entire current fiscal year as approved by Borrower's Board of Directors, which such annual financial projections shall be set forth in a quarter-by-quarter format (such annual financial projections as originally delivered to Collateral Agent and the Lenders are referred to herein as the "**Annual Projections**"); provided that, any revisions of the Annual Projections approved by Borrower's Board of Directors shall be delivered to Collateral Agent and the Lenders no later than seven (7) days after such approval);

(v) within five (5) days of delivery, copies of all statements, reports and notices made available to Borrower's security holders or holders of Subordinated Debt;

(vi) in the event that Borrower continues to be subject to the reporting requirements under the Securities Exchange Act of 1934, as amended, within five (5) days of filing, all reports on Form 10-K, 10-Q and 8-K filed with the Securities and Exchange Commission,

(vii) (a) prompt notice of any amendments of or other changes to the Operating Documents of Borrower or any of its Subsidiaries, (b) in the event that Borrower is no longer subject to the reporting requirements under the Securities Exchange Act of 1934, as amended, prompt notice of any material changes to the capitalization of Borrower, together (in the case of both (a) and (b)), with any copies reflecting such amendments or changes with respect thereto;

(viii) prompt notice of any event that could reasonably be expected to materially and adversely affect the value of the Intellectual Property;

(ix) as soon as available, but no later than thirty (30) days after the last day of each month, copies of the month-end account statements for each Collateral Account maintained by Borrower or its Subsidiaries, which statements may be provided to Collateral Agent and each Lender by Borrower or directly from the applicable institution(s); and

(x) other information as reasonably requested by Collateral Agent or any Lender.

Notwithstanding the foregoing, documents required to be delivered pursuant to the terms hereof (to the extent any such documents are included in materials otherwise filed with the SEC) may be delivered electronically and if so delivered, shall be deemed to have been delivered on the date on which Borrower posts such documents on Borrower's website or provides a link thereto on Borrower's website.

(b) Deliver to each Lender a duly completed Compliance Certificate signed by a Responsible Officer concurrently with the delivery of the financial statements specified in Section 6.2(a)(i) above but no later than thirty (30) days after the last day of each month.

(c) Keep proper books of record and account in accordance with GAAP in all material respects, in which full, true and correct entries shall be made of all dealings and transactions in relation to its business and activities. Borrower shall, and shall cause each of its Subsidiaries to, allow, at the sole cost of Borrower, Collateral Agent or any Lender, during regular business hours upon reasonable prior notice (provided that no notice shall be required when an Event of Default has occurred and is continuing), to visit and inspect any of its properties, to examine and make abstracts or copies from any of its books and records, and to conduct a collateral audit and analysis of its operations and the Collateral. Such audits shall be conducted no more often than once every year unless (and more frequently if) an Event of Default has occurred and is continuing.

6.3 Inventory; Returns. Keep all Inventory in good and marketable condition, free from material defects. Returns and allowances between Borrower, or any of its Subsidiaries, and their respective Account Debtors shall follow Borrower's, or such Subsidiary's, customary practices as they exist at the Effective Date. Borrower must promptly notify Collateral Agent and the Lenders of all returns, recoveries, disputes and claims that involve more than Two Hundred Fifty Thousand Dollars (\$250,000.00) individually or in the aggregate in any calendar year.

6.4 Taxes; Pensions. Timely file and require each of its Subsidiaries to timely file, all required tax returns and reports or extensions therefor and timely pay, and require each of its Subsidiaries to timely pay, all foreign, federal, state, and local taxes, assessments, deposits and contributions owed by Borrower or its Subsidiaries, except for deferred payment of any taxes contested pursuant to the terms of Section 5.8 hereof, and shall deliver to Lenders, on demand, appropriate certificates attesting to such payments, and pay all amounts necessary to fund all present pension, profit sharing and deferred compensation plans in accordance with the terms of such plans.

6.5 Insurance. Keep Borrower's and its Subsidiaries' business and the Collateral insured for risks and in amounts standard for companies in Borrower's and its Subsidiaries' industry and location and as Collateral Agent may reasonably request. Insurance policies shall be in a form, with companies, and in amounts that are reasonably satisfactory to Collateral Agent and Lenders. All property policies shall have a lender's loss payable endorsement showing Collateral Agent as lender loss payee and waive subrogation against Collateral Agent, and all liability policies shall show, or have endorsements showing, Collateral Agent, as additional insured. The Collateral Agent shall be named as lender loss payee and/or additional insured with respect to any such insurance providing coverage in respect of any Collateral, and each provider of any such insurance shall agree, by endorsement upon the policy or policies issued by it or by independent instruments furnished to the Collateral Agent, that it will give the Collateral Agent thirty (30) days (ten (10) days for non-payment of premium) prior written notice before any such policy or policies shall be materially altered or canceled. At Collateral Agent's request, Borrower shall deliver certified copies of policies and evidence of all premium payments. Proceeds payable under any policy shall, at Collateral Agent's option, be payable to Collateral Agent, for the ratable benefit of the Lenders, on account of the Obligations. Notwithstanding the foregoing, (a) so long as no Event of Default has occurred and is continuing, Borrower shall have the option of applying the proceeds of any casualty policy up to Two Hundred Fifty Thousand Dollars (\$250,000.00) with respect to any loss, but not exceeding Two Hundred Fifty Thousand Dollars (\$250,000.00), in the aggregate for all losses under all casualty policies in any one year, toward the replacement or repair of destroyed or damaged property; provided that any such replaced or repaired property (i) shall be of equal or like value as the replaced or repaired Collateral and (ii) shall be deemed Collateral in which Collateral Agent has been granted a first priority security interest, and (b) after the occurrence and during the continuance of an Event of Default, all proceeds payable under such casualty policy shall, at the option of Collateral Agent, be payable to Collateral Agent, for the ratable benefit of the Lenders, on account of the Obligations. If Borrower or any of its Subsidiaries fails to obtain insurance as required under this Section 6.5 or to pay any amount or furnish any required proof of payment to third persons, Collateral Agent and/or any Lender may make, at Borrower's expense, all or part of such payment or obtain such insurance policies required in this Section 6.5, and take any action under the policies Collateral Agent or such Lender deems prudent.

6.6 Operating Accounts.

(a) Maintain all of Borrower's and its Subsidiaries' Collateral Accounts in accounts which are subject to a Control Agreement in favor of Collateral Agent (except as provided in Section 6.6(b)).

(b) Borrower shall provide Collateral Agent five (5) days' prior written notice before Borrower or any of its Subsidiaries establishes any new Collateral Account. In addition, for each Collateral Account that Borrower or any of its Subsidiaries, at any time maintains, Borrower or such Subsidiary shall cause the applicable bank or financial institution at or with which such Collateral Account is maintained to execute and deliver a Control Agreement or other appropriate instrument with respect to such Collateral Account to perfect Collateral Agent's Lien in such Collateral Account in accordance with the terms hereunder prior to the establishment of such Collateral Account, which Control Agreement may not be terminated without prior written consent of Collateral Agent. The provisions of the previous sentence shall not apply to deposit accounts exclusively used for payroll, payroll taxes and other employee wage and benefit payments to or for the benefit of Borrower's, or any of its Subsidiaries', employees and identified to Collateral Agent by Borrower as such in the Perfection Certificates. Collateral Agent agrees not to place a "hold" or deliver a notice of exclusive control, entitlement order, or other similar directions or instructions under any Control Agreement or similar agreements providing control of any Collateral unless an Event of Default has occurred.

(c) Neither Borrower nor any of its Subsidiaries shall maintain any Collateral Accounts except Collateral Accounts maintained in accordance with Sections 6.6(a) and (b).

6.7 Protection of Intellectual Property Rights. Borrower and each of its Subsidiaries shall: (a) use commercially reasonable efforts to protect, defend and maintain the validity and enforceability of its Intellectual Property that is material to Borrower's business; (b) promptly advise Collateral Agent in writing upon becoming aware of material infringement by a third party of its Intellectual Property; and (c) not allow any Intellectual Property material to Borrower's business to be abandoned, forfeited or dedicated to the public without Collateral Agent's prior written consent.

6.8 Litigation Cooperation. Commencing on the Effective Date and continuing through the termination of this Agreement, make available to Collateral Agent and the Lenders, without expense to Collateral Agent or the Lenders, Borrower and each of Borrower's officers, employees and agents and Borrower's Books, to the extent that Collateral Agent or any Lender may reasonably deem them necessary to prosecute or defend any third-party suit or proceeding instituted by or against Collateral Agent or any Lender with respect to any Collateral or relating to Borrower.

6.9 Notices of Litigation and Default. Borrower will give prompt written notice to Collateral Agent and the Lenders of any litigation or governmental proceedings pending or threatened (in writing) against Borrower or any of its Subsidiaries, which could reasonably be expected to result in damages or costs to Borrower or any of its Subsidiaries of Two Hundred Fifty Thousand Dollars (\$250,000.00) or more or which could reasonably be expected to have a Material Adverse Change. Without limiting or contradicting any other more specific provision of this Agreement, promptly (and in any event within three (3) Business Days) upon Borrower becoming aware of the existence of any Event of Default or event which, with the giving of notice or passage of time, or both, would constitute an Event of Default, Borrower shall give written notice to Collateral Agent and the Lenders of such occurrence, which such notice shall include a reasonably detailed description of such Event of Default or event which, with the giving of notice or passage of time, or both, would constitute an Event of Default.

6.10 Intentionally Omitted.

6.11 Landlord Waivers; Bailee Waivers. In the event that Borrower or any of its Subsidiaries, after the Effective Date, intends to add any new office or business location, including a warehouse, containing Collateral valued in excess of Two Hundred Fifty Thousand (\$250,000.00) in the aggregate, or otherwise store any portion of the Collateral valued in excess of Two Hundred Fifty Thousand (\$250,000.00) in the aggregate with, or deliver any portion of the Collateral valued in excess of Two Hundred Fifty Thousand (\$250,000.00) in the aggregate to, a bailee, in each case pursuant to Section 7.2, then Borrower or such Subsidiary will first notify the Collateral Agent thereof and, in the event that the new location is the chief executive office of the Borrower or such Subsidiary or the Collateral at any such new location is valued in excess of Two Hundred Fifty Thousand (\$250,000.00) in the aggregate, such bailee or landlord, as applicable, must execute and deliver a bailee waiver or landlord waiver, as applicable, in form and substance reasonably satisfactory to Collateral Agent prior to the addition of any such new office or business location, or any such storage with or delivery to any such bailee, as the case may be. The foregoing paragraph shall not apply to active pharmaceutical ingredient, other raw materials, or concomitant medications intended for use in the Borrower's preclinical or clinical trials.

6.12 Creation/Acquisition of Subsidiaries. In the event Borrower, or any of its Subsidiaries creates or acquires any Subsidiary, Borrower shall provide prior written notice to Collateral Agent and each Lender of the creation or acquisition of such new Subsidiary and take all such action as may be reasonably required by Collateral Agent or any Lender to cause each such Subsidiary to become a co-Borrower hereunder or to guarantee the Obligations of Borrower under the Loan Documents and, in each case, grant a continuing pledge and security interest in and to the assets of such Subsidiary (substantially as described on Exhibit A hereto); and Borrower (or its Subsidiary, as applicable) shall grant and pledge to Collateral Agent, for the ratable benefit of the Lenders, a perfected security interest in the stock, units or other evidence of ownership of each such newly created Subsidiary; provided, however, that solely in the circumstance in which Borrower or any Subsidiary creates or acquires a Foreign Subsidiary in an acquisition permitted by Section 7.7 hereof or otherwise approved by the Required Lenders, (i) such Foreign Subsidiary shall not be required to become a co-Borrower hereunder or to guarantee the Obligations of Borrower under the Loan Documents or grant a continuing pledge and security interest in and to the assets of such Foreign Subsidiary, and (ii) Borrower or any such Subsidiary shall not be required to grant and pledge to Collateral Agent for the ratable benefit of Lenders a perfected security interest in more than sixty-five percent (65%) of the stock, units or other evidence of ownership of such Foreign Subsidiary, if Borrower demonstrates to the reasonable satisfaction of Collateral Agent that such Foreign Subsidiary becoming a co-Borrower or providing such guarantee or pledge and security interest or Borrower or any such Subsidiary providing a perfected security interest in more than sixty-five percent (65%) of the stock, units or other evidence of ownership of such Foreign Subsidiary would create a present and existing adverse tax consequence to Borrower under the U.S. Internal Revenue Code.

6.13 Further Assurances.

(a) Execute any further instruments and take further action as Collateral Agent or any Lender reasonably requests to perfect or continue Collateral Agent's Lien in the Collateral or to effect the purposes of this Agreement.

(b) Deliver to Collateral Agent and Lenders, within five (5) days after the same are sent or received, copies of all material correspondence, reports, documents and other filings with any Governmental Authority that could reasonably be expected to have a material adverse effect on any of the Governmental Approvals material to Borrower's business or otherwise could reasonably be expected to have a Material Adverse Change.

7. NEGATIVE COVENANTS

Borrower shall not, and shall not permit any of its Subsidiaries to, do any of the following without the prior written consent of the Required Lenders:

7.1 Dispositions. Convey, sell, lease, transfer, assign, or otherwise dispose of (collectively, " **Transfer** "), or permit any of its Subsidiaries to Transfer, all or any part of its business or property, except for Transfers (a) of Inventory in the ordinary course of business; (b) of worn out, surplus or obsolete Equipment; (c) in connection with Permitted Liens, Permitted Investments and Permitted Licenses; and (d) other assets of Borrower or its Subsidiaries that do not in the aggregate exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) during any fiscal year.

7.2 Changes in Business, Management, Ownership, or Business Locations. (a) Engage in or permit any of its Subsidiaries to engage in any business other than the businesses engaged in by Borrower as of the Effective Date or reasonably related thereto; (b) liquidate or dissolve; or (c) (i) any Key Person shall cease to be actively engaged in the management of Borrower unless written notice thereof is provided to Collateral Agent within five (5) Business Days of such change, or (ii) suffer or permit a Change in Control. Borrower shall not, without at least ten (10) days' prior written notice to Collateral Agent: (A) add any new office or business location, including a warehouse (unless any such new office or business location (i) contains less than Two Hundred Fifty Thousand Dollars (\$250,000.00) in assets or property of Borrower or any of its Subsidiaries and (ii) is not Borrower's or its Subsidiaries' chief executive office); (B) change its jurisdiction of organization, (C) change its organizational structure or type, (D) change its legal name, or (E) change any organizational number (if any) assigned by its jurisdiction of organization. Collateral Agent agrees not to deliver a notice to a bailee purporting to exercise dominion or control over any Collateral or any other similar direction or instruction under any bailee agreement with Borrower unless an Event of Default has occurred.

7.3 Mergers or Acquisitions. Merge or consolidate, or permit any of its Subsidiaries to merge or consolidate, with any other Person, or acquire, or permit any of its Subsidiaries to acquire, all or substantially all of the capital stock, shares or property of another Person. A Subsidiary may merge or consolidate into another Subsidiary (provided such surviving Subsidiary is a "co-Borrower" hereunder or has provided a secured Guaranty of Borrower's Obligations hereunder) or with (or into) Borrower provided Borrower is the surviving legal entity, and as long as no Event of Default is occurring prior thereto or arises as a result therefrom. Without limiting the foregoing, Borrower shall not, without Collateral Agent's prior written consent, enter into any binding contractual arrangement with any Person to attempt to facilitate a merger or acquisition of Borrower, unless (i) no Event

of Default exists when such agreement is entered into by Borrower, (ii) such agreement does not give such Person the right to claim any fees, payments or damages from Borrower in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00) (except in the event any such right specifically, or such binding contractual arrangement generally, is subject to Borrower's receipt of the Required Lenders' written consent), and (iii) Borrower notifies Collateral Agent in advance of entering into such an agreement.

7.4 Indebtedness. Create, incur, assume, or be liable for any Indebtedness, or permit any Subsidiary to do so, other than Permitted Indebtedness.

7.5 Encumbrance. Create, incur, allow, or suffer any Lien on any of its property, or assign or convey any right to receive income, including the sale of any Accounts, or permit any of its Subsidiaries to do so, except for Permitted Liens, or permit any Collateral not to be subject to the first priority security interest granted herein (except for Permitted Liens that are permitted by the terms of this Agreement to have priority over Collateral Agent's Lien), or enter into any agreement, document, instrument or other arrangement (except with or in favor of Collateral Agent, for the ratable benefit of the Lenders) with any Person which directly or indirectly prohibits or has the effect of prohibiting Borrower, or any of its Subsidiaries, from assigning, mortgaging, pledging, granting a security interest in or upon, or encumbering any of Borrower's or such Subsidiary's Intellectual Property, except as is otherwise permitted in Section 7.1 hereof and the definition of "Permitted Liens" herein.

7.6 Maintenance of Collateral Accounts. Maintain any Collateral Account except pursuant to the terms of Section 6.6 hereof.

7.7 Distributions; Investments. (a) Pay any dividends (other than dividends payable solely in capital stock) or make any distribution or payment in respect of or redeem, retire or purchase any capital stock (other than repurchases pursuant to the terms of employee stock purchase plans, employee restricted stock agreements, stockholder rights plans, director or consultant stock option plans, or similar plans, provided such repurchases do not exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) in the aggregate per fiscal year) or (b) directly or indirectly make any Investment other than Permitted Investments, or permit any of its Subsidiaries to do so. Notwithstanding the foregoing, Subsidiaries of Borrower shall be permitted to pay dividends, or make other distributions, to Borrower.

7.8 Transactions with Affiliates. Directly or indirectly enter into or permit to exist any material transaction with any Affiliate of Borrower or any of its Subsidiaries, except for (a) transactions that are in the ordinary course of Borrower's or such Subsidiary's business, upon fair and reasonable terms that are no less favorable to Borrower or such Subsidiary than would be obtained in an arm's length transaction with a non-affiliated Person, (b) transactions of the type described in and permitted pursuant to be carried out with Affiliates under Section 7.2 or 7.7 hereof, (c) Subordinated Debt or equity investments by Borrower's investors in Borrower or its Subsidiaries, and (d) Investments permitted under sub-clauses (g) or (h) of the definition of Permitted Investments.

7.9 Subordinated Debt. (a) Make or permit any payment on any Subordinated Debt, except under the terms of the subordination, intercreditor, or other similar agreement to which such Subordinated Debt is subject, or (b) amend any provision in any document relating to the Subordinated Debt which would increase the amount thereof, except as permitted under the terms of the subordination, intercreditor, or other similar agreement to which such Subordinated Debt is subject, or adversely affect the subordination thereof to Obligations owed to the Lenders.

7.10 Compliance. Become an "investment company" or a company controlled by an "investment company", under the Investment Company Act of 1940, as amended, or undertake as one of its important activities extending credit to purchase or carry margin stock (as defined in Regulation U of the Board of Governors of the Federal Reserve System), or use the proceeds of any Credit Extension for that purpose; fail to meet the minimum funding requirements of ERISA, permit a Reportable Event or Prohibited Transaction, as defined in ERISA, to occur; fail to comply with the Federal Fair Labor Standards Act or violate any other law or regulation, if the violation could reasonably be expected to have a Material Adverse Change, or permit any of its Subsidiaries to do so; withdraw or permit any Subsidiary to withdraw from participation in, permit partial or complete termination of, or permit the occurrence of any other event with respect to, any present pension, profit sharing and deferred compensation plan which could reasonably be expected to result in any liability of Borrower or any of its Subsidiaries, including any liability to the Pension Benefit Guaranty Corporation or its successors or any other Governmental Authority.

7.11 Compliance with Anti-Terrorism Laws. Collateral Agent hereby notifies Borrower and each of its Subsidiaries that pursuant to the requirements of Anti-Terrorism Laws, and Collateral Agent's policies and practices, Collateral Agent is required to obtain, verify and record certain information and documentation that identifies Borrower and each of its Subsidiaries and their principals, which information includes the name and address of Borrower and each of its Subsidiaries and their principals and such other information that will allow Collateral Agent to identify such party in accordance with Anti-Terrorism Laws. Neither Borrower nor any of its Subsidiaries shall, nor shall Borrower or any of its Subsidiaries permit any Affiliate to, directly or indirectly,

knowingly enter into any documents, instruments, agreements or contracts with any Person listed on the OFAC Lists. Borrower and each of its Subsidiaries shall immediately notify Collateral Agent if Borrower or such Subsidiary has knowledge that Borrower, or any Subsidiary or Affiliate of Borrower, is listed on the OFAC Lists or (a) is convicted on, (b) pleads *nolo contendere* to, (c) is indicted on, or (d) is arraigned and held over on charges involving money laundering or predicate crimes to money laundering. Neither Borrower nor any of its Subsidiaries shall, nor shall Borrower or any of its Subsidiaries, permit any Affiliate to, directly or indirectly, (i) conduct any business or engage in any transaction or dealing with any Blocked Person, including, without limitation, the making or receiving of any contribution of funds, goods or services to or for the benefit of any Blocked Person, (ii) deal in, or otherwise engage in any transaction relating to, any property or interests in property blocked pursuant to Executive Order No. 13224 or any similar executive order or other Anti-Terrorism Law, or (iii) engage in or conspire to engage in any transaction that evades or avoids, or has the purpose of evading or avoiding, or attempts to violate, any of the prohibitions set forth in Executive Order No. 13224 or other Anti-Terrorism Law.

8. EVENTS OF DEFAULT

Any one of the following shall constitute an event of default (an “**Event of Default**”) under this Agreement:

8.1 Payment Default. Borrower fails to (a) make any payment of principal or interest on any Credit Extension on its due date, or (b) pay any other Obligations within three (3) Business Days after such Obligations are due and payable (which three (3) Business Day grace period shall not apply to payments due on the Maturity Date or the date of acceleration pursuant to Section 9.1 (a) hereof). During the cure period, the failure to cure the payment default is not an Event of Default (but no Credit Extension will be made during the cure period);

8.2 Covenant Default.

(a) Borrower or any of its Subsidiaries fails or neglects to perform any obligation in Sections 6.2 (Financial Statements, Reports, Certificates), 6.4 (Taxes; Pensions), 6.5 (Insurance), 6.6 (Operating Accounts), 6.7 (Protection of Intellectual Property Rights), 6.9 (Notice of Litigation and Default), 6.11 (Landlord Waivers; Bailee Waivers), 6.12 (Creation/Acquisition of Subsidiaries) or 6.13 (Further Assurances) or Borrower violates any covenant in Section 7; or

(b) Borrower, or any of its Subsidiaries, fails or neglects to perform, keep, or observe any other term, provision, condition, covenant or agreement contained in this Agreement or any Loan Documents, and as to any default (other than those specified in this Section 8) under such other term, provision, condition, covenant or agreement that can be cured, has failed to cure the default within ten (10) days after the occurrence thereof; provided, however, that if the default cannot by its nature be cured within the ten (10) day period or cannot after diligent attempts by Borrower be cured within such ten (10) day period, and such default is likely to be cured within a reasonable time, then Borrower shall have an additional period (which shall not in any case exceed thirty (30) days) to attempt to cure such default, and within such reasonable time period the failure to cure the default shall not be deemed an Event of Default (but no Credit Extensions shall be made during such cure period). Grace periods provided under this Section shall not apply, among other things, to financial covenants or any other covenants set forth in subsection (a) above;

8.3 Material Adverse Change. A Material Adverse Change occurs;

8.4 Attachment; Levy; Restraint on Business.

(a) (i) The service of process seeking to attach, by trustee or similar process, any funds of Borrower or any of its Subsidiaries or of any entity under control of Borrower or its Subsidiaries on deposit with any Lender or any Lender’s Affiliate or any bank or other institution at which Borrower or any of its Subsidiaries maintains a Collateral Account, or (ii) a notice of lien, levy, or assessment is filed against Borrower or any of its Subsidiaries or their respective assets by any government agency, and the same under subclauses (i) and (ii) hereof are not, within ten (10) days after the occurrence thereof, discharged or stayed (whether through the posting of a bond or otherwise); provided, however, no Credit Extensions shall be made during any ten (10) day cure period; and

(b) (i) any material portion of Borrower’s or any of its Subsidiaries’ assets is attached, seized, levied on, or comes into possession of a trustee or receiver, or (ii) any court order enjoins, restrains, or prevents Borrower or any of its Subsidiaries from conducting any part of its business;

8.5 Insolvency. (a) Borrower or any of its Subsidiaries is or becomes Insolvent; (b) Borrower or any of its Subsidiaries begins an Insolvency Proceeding; or (c) an Insolvency Proceeding is begun against Borrower or any of its Subsidiaries

and not dismissed or stayed within forty-five (45) days (but no Credit Extensions shall be made while Borrower or any Subsidiary is Insolvent and/or until any Insolvency Proceeding is dismissed);

8.6 Other Agreements. There is a default in any agreement to which Borrower or any of its Subsidiaries is a party with a third party or parties resulting in a right by such third party or parties, whether or not exercised, to accelerate the maturity of any Indebtedness in an amount in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00) or that could reasonably be expected to have a Material Adverse Change; provided, however, that the Event of Default under this Section 8.6 caused by the occurrence of a breach or default under such other agreement shall be cured or waived for purposes of this Agreement upon Collateral Agent receiving written notice from the party asserting such breach or default of such cure or waiver of the breach or default under such other agreement, if at the time of such cure or waiver under such other agreement (x) Collateral Agent or any Lender has not declared an Event of Default under this Agreement and/or exercised any rights with respect thereto; (y) any such cure or waiver does not result in an Event of Default under any other provision of this Agreement or any Loan Document; and (z) in connection with any such cure or waiver under such other agreement, the terms of any agreement with such third party are not modified or amended in any manner which could in the good faith business judgment of Collateral Agent or Lenders be materially less advantageous to Borrower;

8.7 Judgments. One or more final judgments, orders, or decrees for the payment of money in an amount, individually or in the aggregate, of at least Two Hundred Fifty Thousand Dollars (\$250,000.00) (not covered by independent third-party insurance as to which liability has been accepted by such insurance carrier) shall be rendered against Borrower or any of its Subsidiaries and shall remain unsatisfied, unvacated, or unstayed for a period of ten (10) days after the entry thereof (provided that no Credit Extensions will be made prior to the satisfaction, vacation, or stay of such judgment, order or decree);

8.8 Misrepresentations. Borrower or any of its Subsidiaries or any Person acting for Borrower or any of its Subsidiaries makes any representation, warranty, or other statement now or later in this Agreement, any Loan Document or in any writing delivered to Collateral Agent and/or Lenders or to induce Collateral Agent and/or the Lenders to enter this Agreement or any Loan Document, and such representation, warranty, or other statement is incorrect in any material respect when made;

8.9 Subordinated Debt. A default or breach occurs under any subordination, intercreditor, or other similar agreement, or any agreement regarding Subordinated Indebtedness, between Borrower or any of its Subsidiaries and any creditor of Borrower or any of its Subsidiaries that signed such an agreement with Collateral Agent or the Lenders, or any creditor that has signed such an agreement with Collateral Agent or the Lenders breaches any terms of such agreement;

8.10 Guaranty. (a) Any Guaranty terminates or ceases for any reason to be in full force and effect; (b) any Guarantor does not perform any obligation or covenant under any Guaranty; (c) any circumstance described in Sections 8.3, 8.4, 8.5, 8.7, or 8.8 occurs with respect to any Guarantor, or (d) the death of any Guarantor who is a natural person and the liquidation, winding up, or termination of existence of any Guarantor that is an entity;

8.11 Governmental Approvals. Any Governmental Approval shall have been revoked, rescinded, suspended, modified in an adverse manner, or not renewed in the ordinary course for a full term *and* such revocation, rescission, suspension, modification or non-renewal has resulted in or could reasonably be expected to result in a Material Adverse Change;

8.12 Lien Priority . Any Lien created hereunder or by any other Loan Document shall at any time fail to constitute a valid and perfected Lien on any of the Collateral purported to be secured thereby, subject to no prior or equal Lien, other than Permitted Liens which are permitted to have priority in accordance with the terms of this Agreement;

8.13 Delisting . The shares of common stock of Borrower are delisted from The NASDAQ Global Market because of failure to comply with continued listing standards thereof or due to a voluntary delisting which results in such shares not being listed on any other nationally recognized stock exchange in the United States having listing standards at least as restrictive as The NASDAQ Global Market; or

8.14 Permitted Licenses. The Event of Default described in the definition of “ **Permitted Licenses** ” occurs.

9. RIGHTS AND REMEDIES

9.1 Rights and Remedies.

(a) Upon the occurrence and during the continuance of an Event of Default, Collateral Agent may, and at the written direction of Required Lenders shall, without notice or demand, do any or all of the following: (i) deliver notice of the Event of Default to Borrower, (ii) by notice to Borrower declare all Obligations immediately due and payable (but if an Event of

Default described in Section 8.5 occurs all Obligations shall be immediately due and payable without any action by Collateral Agent or the Lenders) or (iii) by notice to Borrower suspend or terminate the obligations, if any, of the Lenders to advance money or extend credit for Borrower's benefit under this Agreement or under any other agreement between Borrower and Collateral Agent and/or the Lenders (but if an Event of Default described in Section 8.5 occurs all obligations, if any, of the Lenders to advance money or extend credit for Borrower's benefit under this Agreement or under any other agreement between Borrower and Collateral Agent and/or the Lenders shall be immediately terminated without any action by Collateral Agent or the Lenders).

(b) Without limiting the rights of Collateral Agent and the Lenders set forth in Section 9.1(a) above, upon the occurrence and during the continuance of an Event of Default, Collateral Agent shall have the right, at the written direction of the Required Lenders, without notice or demand, to do any or all of the following:

(i) foreclose upon and/or sell or otherwise liquidate, the Collateral;

(ii) apply to the Obligations any (a) balances and deposits of Borrower that Collateral Agent or any Lender holds or controls, or (b) any amount held or controlled by Collateral Agent or any Lender owing to or for the credit or the account of Borrower; and/or

(iii) commence and prosecute an Insolvency Proceeding or consent to Borrower commencing any Insolvency Proceeding.

(c) Without limiting the rights of Collateral Agent and the Lenders set forth in Sections 9.1(a) and (b) above, upon the occurrence and during the continuance of an Event of Default, Collateral Agent shall have the right, without notice or demand, to do any or all of the following:

(i) settle or adjust disputes and claims directly with Account Debtors for amounts on terms and in any order that Collateral Agent considers advisable, notify any Person owing Borrower money of Collateral Agent's security interest in such funds, and verify the amount of such account;

(ii) make any payments and do any acts it considers necessary or reasonable to protect the Collateral and/or its security interest in the Collateral. Borrower shall assemble the Collateral if Collateral Agent requests and make it available in a location as Collateral Agent reasonably designates. Collateral Agent may enter premises where the Collateral is located, take and maintain possession of any part of the Collateral, and pay, purchase, contest, or compromise any Lien which appears to be prior or superior to its security interest and pay all expenses incurred. Borrower grants Collateral Agent a license to enter and occupy any of its premises, without charge, to exercise any of Collateral Agent's rights or remedies;

(iii) ship, reclaim, recover, store, finish, maintain, repair, prepare for sale, and/or advertise for sale, the Collateral. Collateral Agent is hereby granted a non-exclusive, royalty-free license or other right to use, without charge, Borrower's and each of its Subsidiaries' labels, patents, copyrights, mask works, rights of use of any name, trade secrets, trade names, trademarks, service marks, and advertising matter, or any similar property as it pertains to the Collateral, in completing production of, advertising for sale, and selling any Collateral and, in connection with Collateral Agent's exercise of its rights under this Section 9.1, Borrower's and each of its Subsidiaries' rights under all licenses and all franchise agreements inure to Collateral Agent, for the benefit of the Lenders;

(iv) place a "hold" on any account maintained with Collateral Agent or the Lenders and/or deliver a notice of exclusive control, any entitlement order, or other directions or instructions pursuant to any Control Agreement or similar agreements providing control of any Collateral;

(v) demand and receive possession of Borrower's Books;

(vi) appoint a receiver to seize, manage and realize any of the Collateral, and such receiver shall have any right and authority as any competent court will grant or authorize in accordance with any applicable law, including any power or authority to manage the business of Borrower or any of its Subsidiaries; and

(vii) subject to clauses 9.1(a) and (b), exercise all rights and remedies available to Collateral Agent and each Lender under the Loan Documents or at law or equity, including all remedies provided under the Code (including disposal of the Collateral pursuant to the terms thereof).

Notwithstanding any provision of this Section 9.1 to the contrary, upon the occurrence of any Event of Default, Collateral Agent shall have the right to exercise any and all remedies referenced in this Section 9.1 without the written consent of Required Lenders

following the occurrence of an Exigent Circumstance. As used in the immediately preceding sentence, “**Exigent Circumstance**” means any event or circumstance that, in the reasonable judgment of Collateral Agent, imminently threatens the ability of Collateral Agent to realize upon all or any material portion of the Collateral, such as, without limitation, fraudulent removal, concealment, or abscondment thereof, destruction or material waste thereof, or failure of Borrower or any of its Subsidiaries after reasonable demand to maintain or reinstate adequate casualty insurance coverage, or which, in the judgment of Collateral Agent, could reasonably be expected to result in a material diminution in value of the Collateral.

9.2 Power of Attorney. Borrower hereby irrevocably appoints Collateral Agent as its lawful attorney-in-fact, exercisable upon the occurrence and during the continuance of an Event of Default, to: (a) endorse Borrower’s or any of its Subsidiaries’ name on any checks or other forms of payment or security; (b) sign Borrower’s or any of its Subsidiaries’ name on any invoice or bill of lading for any Account or drafts against Account Debtors; (c) settle and adjust disputes and claims about the Accounts directly with Account Debtors, for amounts and on terms Collateral Agent determines reasonable; (d) make, settle, and adjust all claims under Borrower’s insurance policies; (e) pay, contest or settle any Lien, charge, encumbrance, security interest, and adverse claim in or to the Collateral, or any judgment based thereon, or otherwise take any action to terminate or discharge the same; and (f) transfer the Collateral into the name of Collateral Agent or a third party as the Code or any applicable law permits. Borrower hereby appoints Collateral Agent as its lawful attorney-in-fact to sign Borrower’s or any of its Subsidiaries’ name on any documents necessary to perfect or continue the perfection of Collateral Agent’s security interest in the Collateral regardless of whether an Event of Default has occurred until all Obligations (other than inchoate indemnity obligations) have been satisfied in full and Collateral Agent and the Lenders are under no further obligation to make Credit Extensions hereunder. Collateral Agent’s foregoing appointment as Borrower’s or any of its Subsidiaries’ attorney in fact, and all of Collateral Agent’s rights and powers, coupled with an interest, are irrevocable until all Obligations (other than inchoate indemnity obligations) have been fully repaid and performed and Collateral Agent’s and the Lenders’ obligation to provide Credit Extensions terminates.

9.3 Protective Payments. If Borrower or any of its Subsidiaries fail to obtain the insurance called for by Section 6.5 or fails to pay any premium thereon or fails to pay any other amount which Borrower or any of its Subsidiaries is obligated to pay under this Agreement or any other Loan Document, Collateral Agent may obtain such insurance or make such payment, and all amounts so paid by Collateral Agent are Lenders’ Expenses and immediately due and payable, bearing interest at the Default Rate, and secured by the Collateral. Collateral Agent will make reasonable efforts to provide Borrower with notice of Collateral Agent obtaining such insurance or making such payment at the time it is obtained or paid or within a reasonable time thereafter. No such payments by Collateral Agent are deemed an agreement to make similar payments in the future or Collateral Agent’s waiver of any Event of Default.

9.4 Application of Payments and Proceeds. Notwithstanding anything to the contrary contained in this Agreement, upon the occurrence and during the continuance of an Event of Default, (a) Borrower irrevocably waives the right to direct the application of any and all payments at any time or times thereafter received by Collateral Agent from or on behalf of Borrower or any of its Subsidiaries of all or any part of the Obligations, and, as between Borrower on the one hand and Collateral Agent and Lenders on the other, Collateral Agent shall have the continuing and exclusive right to apply and to reapply any and all payments received against the Obligations in such manner as Collateral Agent may deem advisable notwithstanding any previous application by Collateral Agent, and (b) the proceeds of any sale of, or other realization upon all or any part of the Collateral shall be applied: first, to the Lenders’ Expenses; second, to accrued and unpaid interest on the Obligations (including any interest which, but for the provisions of the United States Bankruptcy Code, would have accrued on such amounts); third, to the principal amount of the Obligations outstanding; and fourth, to any other indebtedness or obligations of Borrower owing to Collateral Agent or any Lender under the Loan Documents. Any balance remaining shall be delivered to Borrower or to whoever may be lawfully entitled to receive such balance or as a court of competent jurisdiction may direct. In carrying out the foregoing, (x) amounts received shall be applied in the numerical order provided until exhausted prior to the application to the next succeeding category, and (y) each of the Persons entitled to receive a payment in any particular category shall receive an amount equal to its pro rata share of amounts available to be applied pursuant thereto for such category. Any reference in this Agreement to an allocation between or sharing by the Lenders of any right, interest or obligation “ratably,” “proportionally” or in similar terms shall refer to Pro Rata Share unless expressly provided otherwise. Collateral Agent, or if applicable, each Lender, shall promptly remit to the other Lenders such sums as may be necessary to ensure the ratable repayment of each Lender’s portion of any Term Loan and the ratable distribution of interest, fees and reimbursements paid or made by Borrower. Notwithstanding the foregoing, a Lender receiving a scheduled payment shall not be responsible for determining whether the other Lenders also received their scheduled payment on such date; provided, however, if it is later determined that a Lender received more than its ratable share of scheduled payments made on any date or dates, then such Lender shall remit to Collateral Agent or other Lenders such sums as may be necessary to ensure the ratable payment of such scheduled payments, as instructed by Collateral Agent. If any payment or distribution of any kind or character, whether in cash, properties or securities, shall be received by a Lender in excess of its ratable share, then the portion of such payment or distribution in excess of such Lender’s ratable share shall be received by such Lender in trust for and shall be promptly paid over to the other Lender for application to the payments of amounts due on the other Lenders’ claims. To the extent any payment for the account of Borrower is required to be returned as a voidable transfer or otherwise, the Lenders

shall contribute to one another as is necessary to ensure that such return of payment is on a pro rata basis. If any Lender shall obtain possession of any Collateral, it shall hold such Collateral for itself and as agent and bailee for Collateral Agent and other Lenders for purposes of perfecting Collateral Agent's security interest therein.

9.5 Liability for Collateral. So long as Collateral Agent and the Lenders comply with reasonable banking practices regarding the safekeeping of the Collateral in the possession or under the control of Collateral Agent and the Lenders, Collateral Agent and the Lenders shall not be liable or responsible for: (a) the safekeeping of the Collateral; (b) any loss or damage to the Collateral; (c) any diminution in the value of the Collateral; or (d) any act or default of any carrier, warehouseman, bailee, or other Person. Subject to the immediately preceding sentence, Borrower bears all risk of loss, damage or destruction of the Collateral.

9.6 No Waiver; Remedies Cumulative. Failure by Collateral Agent or any Lender, at any time or times, to require strict performance by Borrower of any provision of this Agreement or any other Loan Document shall not waive, affect, or diminish any right of Collateral Agent or any Lender thereafter to demand strict performance and compliance herewith or therewith. No waiver hereunder shall be effective unless signed by Collateral Agent and the Required Lenders and then is only effective for the specific instance and purpose for which it is given. The rights and remedies of Collateral Agent and the Lenders under this Agreement and the other Loan Documents are cumulative. Collateral Agent and the Lenders have all rights and remedies provided under the Code, any applicable law, by law, or in equity. The exercise by Collateral Agent or any Lender of one right or remedy is not an election, and Collateral Agent's or any Lender's waiver of any Event of Default is not a continuing waiver. Collateral Agent's or any Lender's delay in exercising any remedy is not a waiver, election, or acquiescence.

9.7 Demand Waiver. Borrower waives, to the fullest extent permitted by law, demand, notice of default or dishonor, notice of payment and nonpayment, notice of any default, nonpayment at maturity, release, compromise, settlement, extension, or renewal of accounts, documents, instruments, chattel paper, and guarantees held by Collateral Agent or any Lender on which Borrower or any Subsidiary is liable.

10. NOTICES

All notices, consents, requests, approvals, demands, or other communication (collectively, "**Communication**") by any party to this Agreement or any other Loan Document must be in writing and shall be deemed to have been validly served, given, or delivered: (a) upon the earlier of actual receipt and three (3) Business Days after deposit in the U.S. mail, first class, registered or certified mail return receipt requested, with proper postage prepaid; (b) upon transmission, when sent by electronic mail (if an email address is specified herein) or facsimile transmission; (c) one (1) Business Day after deposit with a reputable overnight courier with all charges prepaid; or (d) when delivered, if hand-delivered by messenger, all of which shall be addressed to the party to be notified and sent to the address, facsimile number, or email address indicated below. Any of Collateral Agent, Lender or Borrower may change its mailing address, e-mail address, or facsimile number by giving the other party written notice thereof in accordance with the terms of this Section 10.

If to Borrower: REGULUS THERAPEUTICS INC.
10614 Science Center Dr.
San Diego, California 92121
Attn: Joseph Hagan and Dan Chevallard
Email: jhagan@regulusrx.com and
dchevallard@regulusrx.com

with a copy (which shall not
constitute notice) to: Cooley LLP
4401 Eastgate Mall
San Diego, California 92121
Attn: Kenneth J. Rollins
Fax: (858) 550-6420
Email: krollins@cooley.com

If to Collateral Agent: OXFORD FINANCE LLC
133 North Fairfax Street
Alexandria, Virginia 22314
Attention: Legal Department
Fax: (703) 519-5225
Email: LegalDepartment@oxfordfinance.com

with a copy (which shall not
constitute notice) to: Greenberg Traurig, LLP
One International Place
Boston, MA 02110
Attn: Jonathan Bell, Esq.
Fax: (617) 310-6001
Email: bellj@gtlaw.com

11. CHOICE OF LAW, VENUE AND JURY TRIAL WAIVER, AND JUDICIAL REFERENCE

California law governs the Loan Documents without regard to principles of conflicts of law. Borrower, Collateral Agent and each Lender each submit to the exclusive jurisdiction of the State and Federal courts in Santa Clara County, California; provided, however, that nothing in this Agreement shall be deemed to operate to preclude Collateral Agent or any Lender from bringing suit or taking other legal action in any other jurisdiction to realize on the Collateral or any other security for the Obligations, or to enforce a judgment or other court order in favor of Collateral Agent or any Lender. Borrower expressly submits and consents in advance to such jurisdiction in any action or suit commenced in any such court, and Borrower hereby waives any objection that it may have based upon lack of personal jurisdiction, improper venue, or forum non conveniens and hereby consents to the granting of such legal or equitable relief as is deemed appropriate by such court. Borrower hereby waives personal service of the summons, complaints, and other process issued in such action or suit and agrees that service of such summons, complaints, and other process may be made by registered or certified mail addressed to Borrower at the address set forth in, or subsequently provided by Borrower in accordance with, Section 10 of this Agreement and that service so made shall be deemed completed upon the earlier to occur of Borrower's actual receipt thereof or three (3) days after deposit in the U.S. mails, proper postage prepaid.

TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, BORROWER, COLLATERAL AGENT AND EACH LENDER EACH WAIVE THEIR RIGHT TO A JURY TRIAL OF ANY CLAIM OR CAUSE OF ACTION ARISING OUT OF OR BASED UPON THIS AGREEMENT, THE LOAN DOCUMENTS OR ANY CONTEMPLATED TRANSACTION, INCLUDING CONTRACT, TORT, BREACH OF DUTY AND ALL OTHER CLAIMS. THIS WAIVER IS A MATERIAL INDUCEMENT FOR EACH PARTY TO ENTER INTO THIS AGREEMENT. EACH PARTY HAS REVIEWED THIS WAIVER WITH ITS COUNSEL.

WITHOUT INTENDING IN ANY WAY TO LIMIT THE PARTIES' AGREEMENT TO WAIVE THEIR RESPECTIVE RIGHT TO A TRIAL BY JURY, if the above waiver of the right to a trial by jury is not enforceable, the parties hereto agree that any and all disputes or controversies of any nature between them arising at any time shall be decided by a reference to a private judge, mutually selected by the parties (or, if they cannot agree, by the Presiding Judge of the Santa Clara County, California Superior Court) appointed in accordance with California Code of Civil Procedure Section 638 (or pursuant to comparable provisions of federal law if the dispute falls within the exclusive jurisdiction of the federal courts), sitting without a jury, in Santa Clara County, California; and the parties hereby submit to the jurisdiction of such court. The reference proceedings shall be conducted pursuant to and in accordance with the provisions of California Code of Civil Procedure §§ 638 through 645.1, inclusive. The private judge shall have the power, among others, to grant provisional relief, including without limitation, entering temporary restraining orders, issuing preliminary and permanent injunctions and appointing receivers. All such proceedings shall be closed to the public and confidential and all records relating thereto shall be permanently sealed. If during the course of any dispute, a party desires to seek provisional relief, but a judge has not been appointed at that point pursuant to the judicial reference procedures, then such party may apply to the Santa Clara County, California Superior Court for such relief. The proceeding before the private judge shall be conducted in the same manner as it would be before a court under the rules of evidence applicable to judicial proceedings. The parties shall be entitled to discovery which shall be conducted in the same manner as it would be before a court under the rules of discovery applicable to judicial proceedings. The private judge shall oversee discovery and may enforce all discovery rules and orders applicable to judicial proceedings in the same manner as a trial court judge. The parties agree that the selected or appointed private judge shall have the power to decide all issues in the action or proceeding, whether of fact or of law, and shall report a statement of decision thereon pursuant to California Code of Civil Procedure § 644(a). Nothing in this paragraph shall limit the right of any party at any time to exercise self-help remedies, foreclose against collateral, or obtain provisional remedies. The private judge shall also determine all issues relating to the applicability, interpretation, and enforceability of this paragraph.

12. GENERAL PROVISIONS

12.1 Successors and Assigns. This Agreement binds and is for the benefit of the successors and permitted assigns of each party. Borrower may not transfer, pledge or assign this Agreement or any rights or obligations under it without Collateral Agent's and each Lender's prior written consent (which may be granted or withheld in Collateral Agent's and each Lender's discretion, subject to Section 12.6). The Lenders have the right, without the consent of or notice to Borrower, to sell, transfer, assign, pledge, negotiate, or grant participation in (**any** such sale, transfer, assignment, negotiation, or grant of a participation, a "**Lender Transfer**") all or any part of, or any interest in, the Lenders' obligations, rights, and benefits under this Agreement and the other Loan Documents; *provided, however*, that any such Lender Transfer (other than a transfer, pledge, sale or assignment to an Eligible Assignee) of its obligations, rights, and benefits under this Agreement and the other Loan Documents shall require the prior written consent of the Required Lenders (such approved assignee, an "**Approved Lender**"). Borrower and Collateral Agent shall be entitled to continue to deal solely and directly with such Lender in connection with the interests so assigned until Collateral Agent shall have received and accepted an effective assignment agreement in form satisfactory to Collateral Agent executed, delivered and fully completed by the applicable parties thereto, and shall have received such other information regarding such Eligible Assignee or Approved Lender as Collateral Agent reasonably shall require. Notwithstanding anything to the contrary contained herein, so long as no Event of Default has occurred and is continuing, no Lender Transfer (other than a Lender Transfer (i) in connection with (x) assignments by a Lender due to a forced divestiture at the request of any regulatory agency; or (y) upon the occurrence of a default, event of default or similar occurrence with respect to a Lender's own financing or securitization transactions) shall be permitted, without Borrower's consent, to any Person which is an Affiliate or Subsidiary of Borrower, a direct competitor of Borrower or a vulture hedge fund, each as determined by Collateral Agent.

12.2 Indemnification. Borrower agrees to indemnify, defend and hold Collateral Agent and the Lenders and their respective directors, officers, employees, agents, attorneys, or any other Person affiliated with or representing Collateral Agent or the Lenders (each, an "**Indemnified Person**") harmless against: (a) all obligations, demands, claims, and liabilities (collectively, "**Claims**") asserted by any other party in connection with; related to; following; or arising from, out of or under, the transactions contemplated by the Loan Documents; and (b) all losses or Lenders' Expenses incurred, or paid by Indemnified Person in connection with; related to; following; or arising from, out of or under, the transactions contemplated by the Loan Documents between Collateral Agent, and/or the Lenders and Borrower (including reasonable attorneys' fees and expenses), except as to (a) or (b) for Claims and/or losses and/or expenses (including Lenders' Expenses) directly caused by such Indemnified Person's gross negligence or willful misconduct. Borrower hereby further indemnifies, defends and holds each Indemnified Person harmless from and against any and all liabilities, obligations, losses, damages, penalties, actions, judgments, suits, claims, costs, expenses and disbursements of any kind or nature whatsoever (including the fees and disbursements of counsel for such Indemnified Person) in connection with any investigative, response, remedial, administrative or judicial matter or proceeding, whether or not such Indemnified Person shall be designated a party thereto and including any such proceeding initiated by or on behalf of Borrower, and the reasonable expenses of investigation by engineers, environmental consultants and similar technical personnel and any commission, fee or compensation claimed by any broker (other than any broker retained by Collateral Agent or Lenders) asserting any right to payment for the transactions contemplated hereby which may be imposed on, incurred by or asserted against such

Indemnified Person as a result of or in connection with the transactions contemplated hereby and the use or intended use of the proceeds of the loan proceeds except for liabilities, obligations, losses, damages, penalties, actions, judgments, suits, claims, costs, expenses and disbursements directly caused by such Indemnified Person's gross negligence or willful misconduct.

12.3 Time of Essence. Time is of the essence for the performance of all Obligations in this Agreement.

12.4 Severability of Provisions. Each provision of this Agreement is severable from every other provision in determining the enforceability of any provision.

12.5 Correction of Loan Documents. Collateral Agent and the Lenders may correct patent errors and fill in any blanks in this Agreement and the other Loan Documents in a manner consistent with the agreement of the parties so long as Collateral Agent provides Borrower with written notice of such correction and allows Borrower at least ten (10) days to object to such correction. In the event of such objection, such correction shall not be made except by an amendment signed by both Collateral Agent and Borrower.

12.6 Amendments in Writing; Integration. (a) No amendment, modification, termination or waiver of any provision of this Agreement or any other Loan Document, no approval or consent thereunder, or any consent to any departure by Borrower or any of its Subsidiaries therefrom, shall in any event be effective unless the same shall be in writing and signed by Borrower, Collateral Agent and the Required Lenders provided that:

(i) no such amendment, waiver or other modification that would have the effect of increasing or reducing a Lender's Term Loan Commitment or Commitment Percentage shall be effective as to such Lender without such Lender's written consent;

(ii) no such amendment, waiver or modification that would affect the rights and duties of Collateral Agent shall be effective without Collateral Agent's written consent or signature;

(iii) no such amendment, waiver or other modification shall, unless signed by all the Lenders directly affected thereby, (A) reduce the principal of, rate of interest on or any fees with respect to any Term Loan or forgive any principal, interest (other than default interest) or fees (other than late charges) with respect to any Term Loan (B) postpone the date fixed for, or waive, any payment of principal of any Term Loan or of interest on any Term Loan (other than default interest) or any fees provided for hereunder (other than late charges or for any termination of any commitment); (C) change the definition of the term " **Required Lenders** " or the percentage of Lenders which shall be required for the Lenders to take any action hereunder; (D) release all or substantially all or any material portion of the Collateral, authorize Borrower to sell or otherwise dispose of all or substantially all or any material portion of the Collateral or release any Guarantor of all or any portion of the Obligations or its guaranty obligations with respect thereto, except, in each case with respect to this clause (D), as otherwise may be expressly permitted under this Agreement or the other Loan Documents (including in connection with any disposition permitted hereunder); (E) amend, waive or otherwise modify this Section 12.6 or the definitions of the terms used in this Section 12.6 insofar as the definitions affect the substance of this Section 12.6; (F) consent to the assignment, delegation or other transfer by Borrower of any of its rights and obligations under any Loan Document or release Borrower of its payment obligations under any Loan Document, except, in each case with respect to this clause (F), pursuant to a merger or consolidation permitted pursuant to this Agreement; (G) amend any of the provisions of Section 9.4 or amend any of the definitions of Pro Rata Share, Term Loan Commitment, Commitment Percentage or that provide for the Lenders to receive their Pro Rata Shares of any fees, payments, setoffs or proceeds of Collateral hereunder; (H) subordinate the Liens granted in favor of Collateral Agent securing the Obligations; or (I) amend any of the provisions of Section 12.10. It is hereby understood and agreed that all Lenders shall be deemed directly affected by an amendment, waiver or other modification of the type described in the preceding clauses (C), (D), (E), (F), (G) and (H) of the preceding sentence;

(iv) the provisions of the foregoing clauses (i), (ii) and (iii) are subject to the provisions of any interlender or agency agreement among the Lenders and Collateral Agent pursuant to which any Lender may agree to give its consent in connection with any amendment, waiver or modification of the Loan Documents only in the event of the unanimous agreement of all Lenders.

(b) Other than as expressly provided for in Section 12.6(a)(i)-(iii), Collateral Agent may, if requested by the Required Lenders, from time to time designate covenants in this Agreement less restrictive by notification to a representative of Borrower.

(c) This Agreement and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements. All prior agreements, understandings, representations, warranties, and negotiations

between the parties about the subject matter of this Agreement and the Loan Documents merge into this Agreement and the Loan Documents.

12.7 Counterparts. This Agreement may be executed in any number of counterparts and by different parties on separate counterparts, each of which, when executed and delivered, is an original, and all taken together, constitute one Agreement.

12.8 Survival. So long as the Collateral Agent agrees that Borrower has indefeasibly satisfied the Obligations (other than inchoate indemnity obligations and any other obligations which, by their terms, are to survive the termination of this Agreement), in full, in cash, this Agreement may be terminated prior to the Maturity Date by Borrower, effective five (5) Business Days after written notice of termination is given to Collateral Agent. All covenants, representations and warranties made in this Agreement continue in full force and effect until this Agreement has terminated pursuant to its terms and all Obligations (other than inchoate indemnity obligations and any other obligations which, by their terms, are to survive the termination of this Agreement) have been satisfied. The obligation of Borrower in Section 12.2 to indemnify each Lender and Collateral Agent, as well as the confidentiality provisions in Section 12.9 below, shall survive until the statute of limitations with respect to such claim or cause of action shall have run.

12.9 Confidentiality. In handling any confidential information of Borrower, the Lenders and Collateral Agent shall exercise the same degree of care that it exercises for their own proprietary information, but disclosure of information may be made: (a) subject to the terms and conditions of this Agreement, to the Lenders' and Collateral Agent's Subsidiaries or Affiliates, or in connection with a Lender's own financing or securitization transactions and upon the occurrence of a default, event of default or similar occurrence with respect to such financing or securitization transaction; (b) to prospective transferees (other than those identified in (a) above) or purchasers of any interest in the Credit Extensions (provided, however, the Lenders and Collateral Agent shall, except upon the occurrence and during the continuance of an Event of Default, obtain such prospective transferee's or purchaser's agreement to the terms of this provision or to similar confidentiality terms); (c) as required by law, regulation, subpoena, or other order; (d) to Lenders' or Collateral Agent's regulators or as otherwise required in connection with an examination or audit; (e) as Collateral Agent reasonably considers appropriate in exercising remedies under the Loan Documents; and (f) to third party service providers of the Lenders and/or Collateral Agent so long as such service providers have executed a confidentiality agreement with the Lenders and Collateral Agent with terms no less restrictive than those contained herein. Confidential information does not include information that either: (i) is in the public domain or in the Lenders' and/or Collateral Agent's possession when disclosed to the Lenders and/or Collateral Agent, or becomes part of the public domain after disclosure to the Lenders and/or Collateral Agent through no fault of Lenders and/or Collateral Agent; or (ii) is disclosed to the Lenders and/or Collateral Agent by a third party, if the Lenders and/or Collateral Agent does not know that the third party is prohibited from disclosing the information. Subject to the foregoing provisions of this Section 12.9, Collateral Agent and the Lenders may use confidential information for any purpose, including, without limitation, for the development of client databases, reporting purposes, and market analysis. The provisions of the immediately preceding sentence shall survive the termination of this Agreement. The agreements provided under this Section 12.9 supersede all prior agreements, understanding, representations, warranties, and negotiations between the parties about the subject matter of this Section 12.9.

12.10 Right of Set Off. Borrower hereby grants to Collateral Agent and to each Lender, a lien, security interest and right of set off as security for all Obligations to Collateral Agent and each Lender hereunder, whether now existing or hereafter arising upon and against all deposits, credits, collateral and property, now or hereafter in the possession, custody, safekeeping or control of Collateral Agent or the Lenders or any entity under the control of Collateral Agent or the Lenders (including a Collateral Agent affiliate) or in transit to any of them. At any time after the occurrence and during the continuance of an Event of Default, without demand or notice, Collateral Agent or the Lenders may set off the same or any part thereof and apply the same to any liability or obligation of Borrower even though unmatured and regardless of the adequacy of any other collateral securing the Obligations. ANY AND ALL RIGHTS TO REQUIRE COLLATERAL AGENT TO EXERCISE ITS RIGHTS OR REMEDIES WITH RESPECT TO ANY OTHER COLLATERAL WHICH SECURES THE OBLIGATIONS, PRIOR TO EXERCISING ITS RIGHT OF SETOFF WITH RESPECT TO SUCH DEPOSITS, CREDITS OR OTHER PROPERTY OF BORROWER ARE HEREBY KNOWINGLY, VOLUNTARILY AND IRREVOCABLY WAIVED.

12.11 Cooperation of Borrower. If necessary, Borrower agrees to (i) execute any documents (including new Secured Promissory Notes) reasonably required to effectuate and acknowledge each assignment of a Term Loan Commitment or Loan to an assignee in accordance with Section 12.1, (ii) make Borrower's management available to meet with Collateral Agent and prospective participants and assignees of Term Loan Commitments or Credit Extensions (which meetings shall be conducted no more often than once every twelve months unless an Event of Default has occurred and is continuing), and (iii) assist Collateral Agent or the Lenders in the preparation of information relating to the financial affairs of Borrower as any prospective participant or assignee of a Term Loan Commitment or Term Loan reasonably may request. Subject to the provisions of Section 12.9, Borrower authorizes each Lender to disclose to any prospective participant or assignee of a Term Loan Commitment, any and all information in such Lender's possession concerning Borrower and its financial affairs which has been delivered to such Lender by or on behalf

of Borrower pursuant to this Agreement, or which has been delivered to such Lender by or on behalf of Borrower in connection with such Lender's credit evaluation of Borrower prior to entering into this Agreement.

13. **DEFINITIONS**

13.1 Definitions. As used in this Agreement, the following terms have the following meanings:

“**Account**” is any “account” as defined in the Code with such additions to such term as may hereafter be made, and includes, without limitation, all accounts receivable and other sums owing to Borrower.

“**Account Debtor**” is any “account debtor” as defined in the Code with such additions to such term as may hereafter be made.

“**Affiliate**” of any Person is a Person that owns or controls directly or indirectly the Person, any Person that controls or is controlled by or is under common control with the Person, and each of that Person's senior executive officers, directors, partners and, for any Person that is a limited liability company, that Person's managers and members.

“**Agreement**” is defined in the preamble hereof.

“**Amortization Date**” is July 1, 2018.

“**Annual Projections**” is defined in Section 6.2(a).

“**Anti-Terrorism Laws**” are any laws relating to terrorism or money laundering, including Executive Order No. 13224 (effective September 24, 2001), the USA PATRIOT Act, the laws comprising or implementing the Bank Secrecy Act, and the laws administered by OFAC.

“**Approved Fund**” is any (i) investment company, fund, trust, securitization vehicle or conduit that is (or will be) engaged in making, purchasing, holding or otherwise investing in commercial loans and similar extensions of credit in the ordinary course of its business or (ii) any Person (other than a natural person) which temporarily warehouses loans for any Lender or any entity described in the preceding clause (i) and that, with respect to each of the preceding clauses (i) and (ii), is administered or managed by (a) a Lender, (b) an Affiliate of a Lender or (c) a Person (other than a natural person) or an Affiliate of a Person (other than a natural person) that administers or manages a Lender.

“**Approved Lender**” is defined in Section 12.1.

“**Basic Rate**” is with respect to the Term Loans, the per annum rate of interest (based on a year of three hundred sixty (360) days) equal to the sum of (a) the greater of (i) the thirty (30) day U.S. DOLLAR LIBOR rate reported in The Wall Street Journal on the last Business Day of the month that immediately precedes the month in which the interest will accrue and (ii) forty-four hundredths percent (0.44%) plus (b) Eight and fifty-one hundredths percent (8.51%). Notwithstanding the foregoing, the Basic Rate for the Term A Loans for the period from the Effective Date through and including June 30, 2016 shall be Eight and ninety-six hundredths percent (8.96%).

“**Blocked Person**” is any Person: (a) listed in the annex to, or is otherwise subject to the provisions of, Executive Order No. 13224, (b) a Person owned or controlled by, or acting for or on behalf of, any Person that is listed in the annex to, or is otherwise subject to the provisions of, Executive Order No. 13224, (c) a Person with which any Lender is prohibited from dealing or otherwise engaging in any transaction by any Anti-Terrorism Law, (d) a Person that commits, threatens or conspires to commit or supports “terrorism” as defined in Executive Order No. 13224, or (e) a Person that is named a “specially designated national” or “blocked person” on the most current list published by OFAC or other similar list.

“**Borrower**” is defined in the preamble hereof.

“**Borrower's Books**” are Borrower's or any of its Subsidiaries' books and records including ledgers, federal, and state tax returns, records regarding Borrower's or its Subsidiaries' assets or liabilities, the Collateral, business operations or financial condition, and all computer programs or storage or any equipment containing such information.

“**Business Day**” is any day that is not a Saturday, Sunday or a day on which Collateral Agent is closed.

“ **Cash Equivalents** ” are (a) marketable direct obligations issued or unconditionally guaranteed by the United States or any agency or any State thereof having maturities of not more than one (1) year from the date of acquisition; (b) commercial paper maturing no more than one (1) year after its creation and having the highest rating from either Standard & Poor’s Ratings Group or Moody’s Investors Service, Inc., (c) certificates of deposit maturing no more than one (1) year after issue provided that the account in which any such certificate of deposit is maintained is subject to a Control Agreement in favor of Collateral Agent, and (d) money market funds at least ninety-five percent (95.00%) of the assets of which constitute Cash Equivalents of the kinds described in clauses (a) through (c) of this definition. For the avoidance of doubt, the direct purchase by Borrower or any of its Subsidiaries of any Auction Rate Securities, or purchasing participations in, or entering into any type of swap or other derivative transaction, or otherwise holding or engaging in any ownership interest in any type of Auction Rate Security by Borrower or any of its Subsidiaries shall be conclusively determined by the Lenders as an ineligible Cash Equivalent, and any such transaction shall expressly violate each other provision of this Agreement governing Permitted Investments. Notwithstanding the foregoing, Cash Equivalents does not include and Borrower, and each of its Subsidiaries, are prohibited from purchasing, purchasing participations in, entering into any type of swap or other equivalent derivative transaction, or otherwise holding or engaging in any ownership interest in any type of debt instrument, including, without limitation, any corporate or municipal bonds with a long-term nominal maturity for which the interest rate is reset through a Dutch auction and more commonly referred to as an auction rate security (each, an “ **Auction Rate Security** ”).

“ **Change in Control** ” means any event, transaction, or occurrence as a result of which (a) one or more “persons” (as such term is defined in Sections 3(a)(9) and 13(d)(3) of the Exchange Act), other than a trustee or other fiduciary holding securities under an employee benefit plan of Borrower, is or becomes a beneficial owner (within the meaning Rule 13d-3 promulgated under the Exchange Act), directly or indirectly, of securities of Borrower, representing fifty percent (50%) or more of the combined voting power of Borrower’s then outstanding securities; or (b) during any period of twelve consecutive calendar months, individuals who at the beginning of such period constituted the Board of Directors of Borrower (together with any new directors whose election by the Board of Directors of Borrower was approved by a vote of not less than a majority of the directors then still in office who either were directors at the beginning of such period or whose election or nomination for election was previously so approved) cease for any reason other than death or disability to constitute a majority of the directors then in office.

“ **Claims** ” are defined in Section 12.2.

“ **Code** ” is the Uniform Commercial Code, as the same may, from time to time, be enacted and in effect in the State of California; provided, that, to the extent that the Code is used to define any term herein or in any Loan Document and such term is defined differently in different Articles or Divisions of the Code, the definition of such term contained in Article or Division 9 shall govern; provided further, that in the event that, by reason of mandatory provisions of law, any or all of the attachment, perfection, or priority of, or remedies with respect to, Collateral Agent’s Lien on any Collateral is governed by the Uniform Commercial Code in effect in a jurisdiction other than the State of California, the term “Code” shall mean the Uniform Commercial Code as enacted and in effect in such other jurisdiction solely for purposes of the provisions thereof relating to such attachment, perfection, priority, or remedies and for purposes of definitions relating to such provisions.

“ **Collateral** ” is any and all properties, rights and assets of Borrower described on Exhibit A.

“ **Collateral Account** ” is any Deposit Account, Securities Account, or Commodity Account, or any other bank account maintained by Borrower or any Subsidiary at any time.

“ **Collateral Agent** ” is, Oxford, not in its individual capacity, but solely in its capacity as agent on behalf of and for the benefit of the Lenders.

“ **Commitment Percentage** ” is set forth in Schedule 1.1, as amended from time to time.

“ **Commodity Account** ” is any “commodity account” as defined in the Code with such additions to such term as may hereafter be made.

“ **Communication** ” is defined in Section 10.

“ **Compliance Certificate** ” is that certain certificate in the form attached hereto as Exhibit C.

“ **Contingent Obligation** ” is, for any Person, any direct or indirect liability, contingent or not, of that Person for (a) any indebtedness, lease, dividend, letter of credit or other obligation of another such as an obligation directly or indirectly guaranteed, endorsed, co-made, discounted or sold with recourse by that Person, or for which that Person is directly or indirectly liable; (b) any obligations for undrawn letters of credit for the account of that Person; and (c) all obligations from any interest rate, currency or

commodity swap agreement, interest rate cap or collar agreement, or other agreement or arrangement designated to protect a Person against fluctuation in interest rates, currency exchange rates or commodity prices; but “Contingent Obligation” does not include endorsements in the ordinary course of business. The amount of a Contingent Obligation is the stated or determined amount of the primary obligation for which the Contingent Obligation is made or, if not determinable, the maximum reasonably anticipated liability for it determined by the Person in good faith; but the amount may not exceed the maximum of the obligations under any guarantee or other support arrangement.

“ **Control Agreement** ” is any control agreement entered into among the depository institution at which Borrower or any of its Subsidiaries maintains a Deposit Account or the securities intermediary or commodity intermediary at which Borrower or any of its Subsidiaries maintains a Securities Account or a Commodity Account, Borrower and such Subsidiary, and Collateral Agent pursuant to which Collateral Agent obtains control (within the meaning of the Code) for the benefit of the Lenders over such Deposit Account, Securities Account, or Commodity Account.

“ **Copyrights** ” are any and all copyright rights, copyright applications, copyright registrations and like protections in each work of authorship and derivative work thereof, whether published or unpublished and whether or not the same also constitutes a trade secret.

“ **Credit Extension** ” is any Term Loan or any other extension of credit by Collateral Agent or Lenders for Borrower’s benefit.

“ **Default Rate** ” is defined in Section 2.3(b).

“ **Deposit Account** ” is any “deposit account” as defined in the Code with such additions to such term as may hereafter be made.

“ **Designated Deposit Account** ” is Borrower’s deposit account, account number 3300581583, maintained with Silicon Valley Bank.

“ **Disbursement Letter** ” is that certain form attached hereto as Exhibit B.

“ **Dollars** , ” “ **dollars** ” and “**\$**” each mean lawful money of the United States.

“ **Effective Date** ” is defined in the preamble of this Agreement.

“ **Eligible Assignee** ” is (i) a Lender, (ii) an Affiliate of a Lender, (iii) an Approved Fund and (iv) any commercial bank, savings and loan association or savings bank or any other entity which is an “accredited investor” (as defined in Regulation D under the Securities Act of 1933, as amended) and which extends credit or buys loans as one of its businesses, including insurance companies, mutual funds, lease financing companies and commercial finance companies, in each case, which either (A) has a rating of BBB or higher from Standard & Poor’s Rating Group and a rating of Baa2 or higher from Moody’s Investors Service, Inc. at the date that it becomes a Lender or (B) has total assets in excess of Five Billion Dollars (\$5,000,000,000.00), and in each case of clauses (i) through (iv), which, through its applicable lending office, is capable of lending to Borrower without the imposition of any withholding or similar taxes; provided that notwithstanding the foregoing, “Eligible Assignee” shall not include, unless an Event of Default has occurred and is continuing, (i) Borrower or any of Borrower’s Affiliates or Subsidiaries or (ii) a direct competitor of Borrower or a vulture hedge fund, each as determined by Collateral Agent. Notwithstanding the foregoing, (x) in connection with assignments by a Lender due to a forced divestiture at the request of any regulatory agency, the restrictions set forth herein shall not apply and Eligible Assignee shall mean any Person or party and (y) in connection with a Lender’s own financing or securitization transactions, the restrictions set forth herein shall not apply and Eligible Assignee shall mean any Person or party providing such financing or formed to undertake such securitization transaction and any transferee of such Person or party upon the occurrence of a default, event of default or similar occurrence with respect to such financing or securitization transaction; provided that no such sale, transfer, pledge or assignment under this clause (y) shall release such Lender from any of its obligations hereunder or substitute any such Person or party for such Lender as a party hereto until Collateral Agent shall have received and accepted an effective assignment agreement from such Person or party in form satisfactory to Collateral Agent executed, delivered and fully completed by the applicable parties thereto, and shall have received such other information regarding such Eligible Assignee as Collateral Agent reasonably shall require.

“ **Equipment** ” is all “equipment” as defined in the Code with such additions to such term as may hereafter be made, and includes without limitation all machinery, fixtures, goods, vehicles (including motor vehicles and trailers), and any interest in any of the foregoing.

“ **ERISA** ” is the Employee Retirement Income Security Act of 1974, as amended, and its regulations.

“ **Event of Default** ” is defined in Section 8.

“ **Final Payment** ” is a payment (in addition to and not a substitution for the regular monthly payments of principal plus accrued interest) due on the earliest to occur of (a) the Maturity Date, or (b) the acceleration of any Term Loan, or (c) the prepayment of a Term Loan pursuant to Section 2.2(c) or (d), equal to the original principal amount of such Term Loan multiplied by the Final Payment Percentage, payable to Lenders in accordance with their respective Pro Rata Shares.

“ **Final Payment Percentage** ” is Five and one-half percent (5.50%).

“ **Foreign Subsidiary** ” is a Subsidiary that is not an entity organized under the laws of the United States or any territory thereof.

“ **Funding Date** ” is any date on which a Credit Extension is made to or on account of Borrower which shall be a Business Day.

“ **GAAP** ” is generally accepted accounting principles set forth in the opinions and pronouncements of the Accounting Principles Board of the American Institute of Certified Public Accountants and statements and pronouncements of the Financial Accounting Standards Board or in such other statements by such other Person as may be approved by a significant segment of the accounting profession in the United States, which are applicable to the circumstances as of the date of determination.

“ **General Intangibles** ” are all “general intangibles” as defined in the Code in effect on the date hereof with such additions to such term as may hereafter be made, and includes without limitation, all copyright rights, copyright applications, copyright registrations and like protections in each work of authorship and derivative work, whether published or unpublished, any patents, trademarks, service marks and, to the extent permitted under applicable law, any applications therefor, whether registered or not, any trade secret rights, including any rights to unpatented inventions, payment intangibles, royalties, contract rights, goodwill, franchise agreements, purchase orders, customer lists, route lists, telephone numbers, domain names, claims, income and other tax refunds, security and other deposits, options to purchase or sell real or personal property, rights in all litigation presently or hereafter pending (whether in contract, tort or otherwise), insurance policies (including without limitation key man, property damage, and business interruption insurance), payments of insurance and rights to payment of any kind.

“ **Governmental Approval** ” is any consent, authorization, approval, order, license, franchise, permit, certificate, accreditation, registration, filing or notice, of, issued by, from or to, or other act by or in respect of, any Governmental Authority.

“ **Governmental Authority** ” is any nation or government, any state or other political subdivision thereof, any agency, authority, instrumentality, regulatory body, court, central bank or other entity exercising executive, legislative, judicial, taxing, regulatory or administrative functions of or pertaining to government, any securities exchange and any self-regulatory organization.

“ **Guarantor** ” is any Person providing a Guaranty in favor of Collateral Agent.

“ **Guaranty** ” is any guarantee of all or any part of the Obligations, as the same may from time to time be amended, restated, modified or otherwise supplemented.

“ **Indebtedness** ” is (a) indebtedness for borrowed money or the deferred price of property or services, such as reimbursement and other obligations for surety bonds and letters of credit, (b) obligations evidenced by notes, bonds, debentures or similar instruments, (c) capital lease obligations, and (d) Contingent Obligations.

“ **Indemnified Person** ” is defined in Section 12.2.

“ **Insolvency Proceeding** ” is any proceeding by or against any Person under the United States Bankruptcy Code, or any other bankruptcy or insolvency law, including assignments for the benefit of creditors, compositions, extensions generally with its creditors, or proceedings seeking reorganization, arrangement, or other relief.

“ **Insolvent** ” means not Solvent.

“ **Intellectual Property** ” means all of Borrower’s or any Subsidiary’s right, title and interest in and to the following:

- (a) its Copyrights, Trademarks and Patents;
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- (b) any and all trade secrets and trade secret rights, including, without limitation, any rights to unpatented inventions, know-how, operating manuals;
- (c) trade names, mask works, rights of use of any name, domain names, websites, or any other similar rights, any applications therefor, whether registered or not;
- (d) any and all source code;
- (e) any and all design rights which may be available to Borrower;
- (f) any and all intellectual property rights in computer software and computer software products;
- (g) any and all claims for damages by way of past, present and future infringement of any of the foregoing, with the right, but not the obligation, to sue for and collect such damages for said use or infringement of the Intellectual Property rights identified above; and
- (h) all amendments, renewals and extensions of any of the Copyrights, Trademarks or Patents.

“**Inventory**” is all “inventory” as defined in the Code in effect on the date hereof with such additions to such term as may hereafter be made, and includes without limitation all merchandise, raw materials, parts, supplies, packing and shipping materials, work in process and finished products, including without limitation such inventory as is temporarily out of any Person’s custody or possession or in transit and including any returned goods and any documents of title representing any of the above.

“**Investment**” is any beneficial ownership interest in any Person (including stock, partnership interest or other securities), and any loan, advance, payment or capital contribution to any Person.

“**Key Person**” is each of Borrower’s (i) Chief Executive Officer, who is Paul C. Grint, M.D. as of the Effective Date, and (ii) principal financial officer and Chief Operating Officer, who is Joseph Hagan as of the Effective Date.

“**Lender**” is any one of the Lenders.

“**Lenders**” are the Persons identified on Schedule 1.1 hereto and each assignee that becomes a party to this Agreement pursuant to Section 12.1.

“**Lenders’ Expenses**” are all audit fees and expenses, costs, and expenses (including reasonable attorneys’ fees and expenses, as well as appraisal fees, fees incurred on account of lien searches, inspection fees, and filing fees) for preparing, amending, negotiating, administering, defending and enforcing the Loan Documents (including, without limitation, those incurred in connection with appeals or Insolvency Proceedings) or otherwise incurred by Collateral Agent and/or the Lenders in connection with the Loan Documents.

“**Lien**” is a claim, mortgage, deed of trust, levy, charge, pledge, security interest, or other encumbrance of any kind, whether voluntarily incurred or arising by operation of law or otherwise against any property.

“**Loan Documents**” are, collectively, this Agreement, the Perfection Certificates, each Compliance Certificate, each Disbursement Letter, any subordination agreements, any note, or notes or guaranties executed by Borrower or any other Person, and any other present or future agreement entered into by Borrower, any Guarantor or any other Person for the benefit of the Lenders and Collateral Agent in connection with this Agreement; all as amended, restated, or otherwise modified.

“**Material Adverse Change**” is (a) a material impairment in the perfection or priority of Collateral Agent’s Lien in the Collateral or in the value of such Collateral; (b) a material adverse change in the business, operations or condition (financial or otherwise) of Borrower or any Subsidiary; or (c) a material impairment of the prospect of repayment of any portion of the Obligations.

“**Maturity Date**” is June 1, 2020.

“**Milestone Event**” is achievement of positive interim safety and efficacy data from the Phase 2 clinical trial (in collaboration with GlaxoSmithKline) of Borrower’s drug candidate subcutaneous RG-101 in combination with GlaxoSmithKline’s

oral GSK 175 for treatment of HCV, on or before March 31, 2017, as determined by Collateral Agent based on evidence reasonably acceptable to Collateral Agent.

“ **Obligations** ” are all of Borrower’s obligations to pay when due any debts, principal, interest, Lenders’ Expenses, the Prepayment Fee, the Final Payment, and other amounts Borrower owes the Lenders now or later, in connection with, related to, following, or arising from, out of or under, this Agreement or, the other Loan Documents, or otherwise, and including interest accruing after Insolvency Proceedings begin (whether or not allowed) and debts, liabilities, or obligations of Borrower assigned to the Lenders and/or Collateral Agent, and the performance of Borrower’s duties under the Loan Documents.

“ **OFAC** ” is the U.S. Department of Treasury Office of Foreign Assets Control.

“ **OFAC Lists** ” are, collectively, the Specially Designated Nationals and Blocked Persons List maintained by OFAC pursuant to Executive Order No. 13224, 66 Fed. Reg. 49079 (Sept. 25, 2001) and/or any other list of terrorists or other restricted Persons maintained pursuant to any of the rules and regulations of OFAC or pursuant to any other applicable Executive Orders.

“ **Operating Documents** ” are, for any Person, such Person’s formation documents, as certified by the Secretary of State (or equivalent agency) of such Person’s jurisdiction of organization on a date that is no earlier than thirty (30) days prior to the Funding Date of the Term A Loans, and, (a) if such Person is a corporation, its bylaws in current form, (b) if such Person is a limited liability company, its limited liability company agreement (or similar agreement), and (c) if such Person is a partnership, its partnership agreement (or similar agreement), each of the foregoing with all current amendments or modifications thereto.

“ **Patents** ” means all patents, patent applications and like protections including without limitation improvements, amendments, divisions, continuations, renewals, reissues, extensions and continuations-in-part of the same.

“ **Payment Date** ” is the first (1st) calendar day of each calendar month, commencing on August 1, 2016.

“ **Perfection Certificate** ” and “ **Perfection Certificates** ” is defined in Section 5.1.

“ **Permitted Indebtedness** ” is:

- (a) Borrower’s Indebtedness to the Lenders and Collateral Agent under this Agreement and the other Loan Documents;
- (b) Indebtedness existing on the Effective Date and disclosed on the Perfection Certificate(s);
- (c) Subordinated Debt;
- (d) unsecured Indebtedness to trade creditors incurred in the ordinary course of business;
- (e) Indebtedness consisting of capitalized lease obligations and purchase money Indebtedness, in each case incurred by Borrower or any of its Subsidiaries to finance the acquisition, repair, improvement or construction of fixed or capital assets of such person, provided that (i) the aggregate outstanding principal amount of all such Indebtedness does not exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) at any time and (ii) the principal amount of such Indebtedness does not exceed the lower of the cost or fair market value of the property so acquired or built or of such repairs or improvements financed with such Indebtedness (each measured at the time of such acquisition, repair, improvement or construction is made);
- (f) Indebtedness incurred as a result of endorsing negotiable instruments received in the ordinary course of Borrower’s business;
- (g) Indebtedness that also constitutes a Permitted Investment under clause (g) of the definition of “Permitted Investment”; and
- (h) extensions, refinancings, modifications, amendments and restatements of any items of Permitted Indebtedness (a) through (g) above, provided that the principal amount thereof is not increased and the terms thereof are not modified to impose materially more burdensome terms upon Borrower, or its Subsidiary, as the case may be.

“ **Permitted Investments** ” are:

- (a) Investments disclosed on the Perfection Certificate(s) and existing on the Effective Date;
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- (b) (i) Investments consisting of cash and Cash Equivalents, and (ii) any other Investments permitted by Borrower's investment policy, as amended from time to time, provided that such investment policy (and any such amendment thereto) has been approved in writing by Collateral Agent;
- (c) Investments consisting of the endorsement of negotiable instruments for deposit or collection or similar transactions in the ordinary course of Borrower;
- (d) Investments consisting of deposit accounts or securities accounts in which Collateral Agent has a perfected security interest (except as otherwise provided in Section 6.6);
- (e) Investments in connection with Transfers permitted by Section 7.1;
- (f) Investments consisting of (i) travel advances and employee relocation loans and other employee loans and advances in the ordinary course of business, and (ii) loans to employees, officers or directors relating to the purchase of equity securities of Borrower or its Subsidiaries pursuant to employee stock purchase plans or agreements approved by Borrower's Board of Directors; not to exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) in the aggregate for (i) and (ii) in any fiscal year;
- (g) Investments (i) by Borrower in a Subsidiary that is a co-Borrower or secured guarantor of the Obligations and is not a Foreign Subsidiary, (ii) by Borrower in a Subsidiary that is not a co-Borrower or guarantor of the Obligations up to Two Hundred Fifty Thousand Dollars (\$250,000.00) in the aggregate in any fiscal year, and (iii) by Subsidiaries in Borrower or in a Subsidiary that is a co-Borrower or secured guarantor of the Obligations and is not a Foreign Subsidiary;
- (h) Repurchases of stock from former employees or directors of Borrower under the terms of applicable repurchase agreements in an aggregate amount not to exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) in any fiscal year, provided that no Event of Default has occurred, is continuing or would exist after giving effect to the repurchases;
- (i) Investments (including debt obligations) received in connection with the bankruptcy or reorganization of customers or suppliers and in settlement of delinquent obligations of, and other disputes with, customers or suppliers arising in the ordinary course of business;
- (j) Investments consisting of notes receivable of, or prepaid royalties and other credit extensions, to customers and suppliers who are not Affiliates, in the ordinary course of business; provided that this paragraph (h) shall not apply to Investments of Borrower in any Subsidiary; and
- (k) joint ventures, corporate collaborations, or strategic alliances in the ordinary course of Borrower's business consisting of the licensing of technology constituting Permitted Licenses, the development of technology or the providing of technical support, provided that any cash investments by Borrower do not exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) in the aggregate in any fiscal year.

“ **Permitted Licenses** ” are (A) licenses of over-the-counter software that is commercially available to the public, and (B) non-exclusive and exclusive licenses for the use of the Intellectual Property of Borrower or any of its Subsidiaries entered into in the ordinary course of business, provided, that, with respect to each such license described in clause (B), (i) no Event of Default has occurred or is continuing at the time of entry into such license; (ii) the license constitutes an arm's-length transaction, the terms of which, on their face, (x) do not provide for a sale or assignment of any Intellectual Property and (y) do not restrict the ability of Borrower or any of its Subsidiaries, as applicable, to pledge, grant a security interest in or lien on, or assign or otherwise Transfer any Intellectual Property (unless any such restriction is subject to any rights of the Collateral Agent or the Lenders under this Agreement (as may be amended or restated from time to time, which amendment or restatement may result in granting of Lien to Collateral Agent for the ratable benefit of the Lenders in any or all Intellectual Property of Borrower)); (iii) in the case of any exclusive license, (x) Borrower delivers at least seven (7) days' prior written notice and a brief summary of the terms of the proposed license to Collateral Agent and the Lenders and delivers to Collateral Agent and the Lenders copies of the final executed licensing documents in connection with the exclusive license promptly upon consummation thereof, and (y) except for license agreements in existence as of the Effective Date as set forth on the Perfection Certificate and in the respective forms provided to Collateral Agent prior to the Effective Date, any such license could not result in a legal transfer of title of the licensed property but may be exclusive in respects other than territory and may be exclusive as to territory only as to discrete geographical areas outside of the United States and may be exclusive in the United States only with the prior written consent of Collateral Agent, except for licenses with respect to Borrower's drug candidate RG-101, for which Collateral Agent's prior written consent shall not be required so long as at least seven (7) days' prior written notice is provided before entering into any exclusive license agreement with respect to Borrower's drug candidate RG-101 and that such license agreement provides for non-contingent cash payment(s) of not less than Fifty Million Dollars (\$50,000,000.00) in the aggregate to be paid to Borrower (and deposited in

accordance with clause (iv) hereof) from the applicable licensee within 90 days following the effective date of such license agreement (and the license agreement provides Borrower with the right to terminate the license immediately, without penalty, upon notice to the applicable licensee in the event such payments are not received by Borrower within such 90-day period; provided, however, Borrower's failure to terminate such license if Borrower has not received non-contingent cash payment(s) of at least Fifty Million Dollars (\$50,000,000.00) provided for in the license agreement within such 90-day period shall be an Event of Default under the Agreement); and (iv) all upfront payments, royalties, milestone payments or other proceeds arising from the licensing agreement that are payable to Borrower or any of its Subsidiaries are paid to a Deposit Account that is governed by a Control Agreement. For purposes of this definition, "licenses" includes sublicenses.

" **Permitted Liens** " are:

- (a) Liens existing on the Effective Date and disclosed on the Perfection Certificates or arising under this Agreement and the other Loan Documents;
 - (b) Liens for taxes, fees, assessments or other government charges or levies, either (i) not due and payable or (ii) being contested in good faith and for which Borrower maintains adequate reserves on its Books, provided that no notice of any such Lien has been filed or recorded under the Internal Revenue Code of 1986, as amended, and the Treasury Regulations adopted thereunder;
 - (c) liens securing Indebtedness permitted under clause (e) of the definition of " **Permitted Indebtedness** ," provided that (i) such liens exist prior to the acquisition of, or attach substantially simultaneous with, or within twenty (20) days after the, acquisition, lease, repair, improvement or construction of, such property financed or leased by such Indebtedness and (ii) such liens do not extend to any property of Borrower other than the property (and proceeds thereof) acquired, leased or built, or the improvements or repairs, financed by such Indebtedness;
 - (d) statutory Liens securing claims or demands of materialmen, mechanics, carriers, warehousemen, landlords and other Persons imposed without action of such parties, provided the aggregate amount of the obligations secured by such Liens does not any time exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) and which are not delinquent or remain payable without penalty or which are being contested in good faith and by appropriate proceedings which proceedings have the effect of preventing the forfeiture or sale of the property subject thereto;
 - (e) Liens to secure payment of workers' compensation, employment insurance, old-age pensions, social security and other like obligations incurred in the ordinary course of business (other than Liens imposed by ERISA);
 - (f) leases or subleases of real property granted in the ordinary course of Borrower's business (or, if referring to another Person, in the ordinary course of such Person's business), and leases, subleases, non-exclusive licenses or sublicenses of personal property (other than Intellectual Property) granted in the ordinary course of Borrower's business (or, if referring to another Person, in the ordinary course of such Person's business), if the leases, subleases, licenses and sublicenses do not prohibit granting Collateral Agent or any Lender a security interest therein;
 - (g) banker's liens, rights of setoff and Liens in favor of financial institutions incurred in the ordinary course of business arising in connection with Borrower's deposit accounts or securities accounts held at such institutions solely to secure payment of fees and similar costs and expenses and provided such accounts are maintained in compliance with Section 6.6(b) hereof;
 - (h) Liens arising from judgments, decrees or attachments in circumstances not constituting an Event of Default under Section 8.4 or 8.7;
 - (i) Liens consisting of Permitted Licenses;
 - (j) deposits to secure the performance of leases incurred in the ordinary course of business and not representing an obligation for borrowed money so long as (1) each such deposit is made at the commencement of a lease or its renewal when there is no underlying default under such lease, and (2) the aggregate amount of all such deposits at any given time does not exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) (excluding deposits to secure the performance of leases disclosed in the Perfection Certificate on the Effective Date);
 - (k) easements, reservations, rights-of-way, restrictions, minor defects or irregularities in title and other similar Liens affecting real property not interfering in any material respect with the ordinary course of the business;
-

(l) deposits (not to exceed in the aggregate an amount of Two Hundred Fifty Thousand Dollars (\$250,000.00) at any given time) to secure the performance of bids, trade contracts (other than for borrowed money), contracts for the purchase of property permitted hereunder, statutory obligations, surety and appeal bonds, performance bonds and other obligations of a like nature, in each case, incurred in the ordinary course of business and not constituting, in the aggregate, obligations in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00) at any given time;

(m) Liens in favor of custom and revenue authorities arising in the ordinary course of business as a matter of law to secure the payment of custom duties in connection with the importation of goods provided such Liens are restricted to the goods being imported and do not exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) at any given time; and

(n) Liens incurred in the extension, renewal or refinancing of the indebtedness secured by Liens described in (a) through (m), but any extension, renewal or replacement Lien must be limited to the property encumbered by the existing Lien and the principal amount of the indebtedness may not increase;

“ **Person** ” is any individual, sole proprietorship, partnership, limited liability company, joint venture, company, trust, unincorporated organization, association, corporation, institution, public benefit corporation, firm, joint stock company, estate, entity or government agency.

“ **Post Closing Letter** ” is that certain Post Closing Letter dated as of the Effective Date by and between Collateral Agent and Borrower.

“ **Prepayment Fee** ” is, with respect to any Term Loan subject to prepayment prior to the Maturity Date, whether by mandatory or voluntary prepayment, acceleration or otherwise, an additional fee payable to the Lenders in amount equal to:

(i) for a prepayment made on or after the Funding Date of such Term Loan through and including the second anniversary of the Funding Date of such Term Loan, two percent (2.00%) of the principal amount of such Term Loan prepaid;

(ii) for a prepayment made after the date which is after the second anniversary of the Funding Date of such Term Loan through and prior to the Maturity Date, one percent (1.00%) of the principal amount of the Term Loan prepaid.

Notwithstanding the foregoing, the “Prepayment Fee” shall be zero percent (0%) of the principal amount of the Term Loans prepaid on or prior to the first anniversary of the Funding Date of the Term A Loan, *if* (A) Borrower merges with or is consolidated into another entity pursuant to which Borrower is not the surviving entity and following which transaction, the stockholders of the Borrower immediately prior to the consummation of such transaction do not own a majority of the voting securities of the surviving entity, (B) in excess of 50% of the Borrower’s voting power is transferred in a transaction or series of related transactions, other than any sale by the Borrower of its stock in one or more transactions the primary purpose of which is to raise capital for the Borrower’s operations, or (C) Borrower sells all or substantially all of its assets, then if such transaction is consummated in accordance with the provisions of this Agreement (an “ **Acquisition Event** ”), and in the case of such Acquisition Event, (i) the Prepayment Fee is not otherwise due hereunder; (ii) Borrower repays all Term Loans advanced by Lenders hereunder and fulfills all other payment Obligations hereunder contemporaneously with the consummation of the Acquisition Event; and (iii) no Event of Default has occurred and is continuing at the time of such Acquisition Event and repayment of Term Loans and fulfillment of all other payment Obligations hereunder. Notwithstanding the foregoing, nothing in this definition or otherwise in this Agreement shall be deemed to be consent to the consummation of an Acquisition Event.

“ **Pro Rata Share** ” is, as of any date of determination, with respect to each Lender, a percentage (expressed as a decimal, rounded to the ninth decimal place) determined by dividing the outstanding principal amount of Term Loans held by such Lender by the aggregate outstanding principal amount of all Term Loans.

“ **Registered Organization** ” is any “registered organization” as defined in the Code with such additions to such term as may hereafter be made.

“ **Required Lenders** ” means (i) for so long as all of the Persons that are Lenders on the Effective Date (each an “ **Original Lender** ”) have not assigned or transferred any of their interests in their Term Loan, Lenders holding one hundred percent (100%) of the aggregate outstanding principal balance of the Term Loan, or (ii) at any time from and after any Original Lender has assigned or transferred any interest in its Term Loan, Lenders holding at least sixty-six percent (66%) of the aggregate outstanding principal balance of the Term Loan and, in respect of this clause (ii), (A) each Original Lender that has not assigned or transferred any portion of its Term Loan, (B) each assignee or transferee of an Original Lender’s interest in the Term Loan, but only to the extent

that such assignee or transferee is an Affiliate or Approved Fund of such Original Lender, and (C) any Person providing financing to any Person described in clauses (A) and (B) above; provided, however, that this clause (C) shall only apply upon the occurrence of a default, event of default or similar occurrence with respect to such financing.

“ **Requirement of Law** ” is as to any Person, the organizational or governing documents of such Person, and any law (statutory or common), treaty, rule or regulation or determination of an arbitrator or a court or other Governmental Authority, in each case applicable to or binding upon such Person or any of its property or to which such Person or any of its property is subject.

“ **Responsible Officer** ” is any of the President, Chief Executive Officer, Chief Operating Officer, Chief Financial Officer, or Vice President of Finance and Accounting of Borrower acting alone.

“ **Second Draw Period** ” is the period commencing on the date of the occurrence of the Milestone Event and ending on the earlier of (i) the date that is sixty (60) days immediately following the date of the occurrence of the Milestone Event, (ii) March 31, 2017 and (iii) the occurrence of an Event of Default; provided, however, that the Second Draw Period shall not commence if on the date of the occurrence of the Milestone Event an Event of Default has occurred and is continuing.

“ **Secured Promissory Note** ” is defined in Section 2.4.

“ **Secured Promissory Note Record** ” is a record maintained by each Lender with respect to the outstanding Obligations owed by Borrower to Lender and credits made thereto.

“ **Securities Account** ” is any “securities account” as defined in the Code with such additions to such term as may hereafter be made.

“ **Solvent** ” is, with respect to any Person: the fair salable value of such Person’s consolidated assets (including goodwill minus disposition costs) exceeds the fair value of such Person’s liabilities; such Person is not left with unreasonably small capital after the transactions in this Agreement; and such Person is able to pay its debts (including trade debts) as they mature.

“ **Subordinated Debt** ” is indebtedness incurred by Borrower or any of its Subsidiaries subordinated to all Indebtedness of Borrower and/or its Subsidiaries to the Lenders (pursuant to a subordination, intercreditor, or other similar agreement in form and substance satisfactory to Collateral Agent and the Lenders entered into between Collateral Agent, Borrower, and/or any of its Subsidiaries, and the other creditor), on terms acceptable to Collateral Agent and the Lenders.

“ **Subsidiary** ” is, with respect to any Person, any Person of which more than fifty percent (50%) of the voting stock or other equity interests (in the case of Persons other than corporations) is owned or controlled, directly or indirectly, by such Person or through one or more intermediaries.

“ **Term Loan** ” is defined in Section 2.2(a)(ii) hereof.

“ **Term A Loan** ” is defined in Section 2.2(a)(i) hereof.

“ **Term B Loan** ” is defined in Section 2.2(a)(ii) hereof.

“ **Term Loan Commitment** ” is, for any Lender, the obligation of such Lender to make a Term Loan, up to the principal amount shown on Schedule 1.1. “ **Term Loan Commitments** ” means the aggregate amount of such commitments of all Lenders.

“ **Trademarks** ” means any trademark and servicemark rights, whether registered or not, applications to register and registrations of the same and like protections, and the entire goodwill of the business of Borrower connected with and symbolized by such trademarks.

“ **Transfer** ” is defined in Section 7.1.

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IN WITNESS WHEREOF , the parties hereto have caused this Agreement to be executed as of the Effective Date.

BORROWER:

REGULUS THERAPEUTICS INC.

By /s/ Paul Grint

Name: Paul Grint

Title: CEO

COLLATERAL AGENT AND LENDER:

OXFORD FINANCE LLC

By /s/ Mark Davis

Name: Mark Davis

Title: Vice President-Finance, Secretary & Treasurer

SCHEDULE 1.1

Lenders and Commitments

Term A Loans

Lender	Term Loan Commitment	Commitment Percentage
OXFORD FINANCE LLC	\$20,000,000	100.00%
TOTAL	\$20,000,000	100.00%

Term B Loans

Lender	Term Loan Commitment	Commitment Percentage
OXFORD FINANCE LLC	\$10,000,000	100.00%
TOTAL	\$10,000,000	100.00%

Aggregate (all Term Loans)

Lender	Term Loan Commitment	Commitment Percentage
OXFORD FINANCE LLC	\$30,000,000	100.00%
TOTAL	\$30,000,000	100.00%

EXHIBIT A

Description of Collateral

The Collateral consists of all of Borrower's right, title and interest in and to the following personal property:

All goods, Accounts (including health-care receivables), Equipment, Inventory, contract rights or rights to payment of money, leases, license agreements, franchise agreements, General Intangibles (except as noted below), commercial tort claims, documents, instruments (including any promissory notes), chattel paper (whether tangible or electronic), cash, deposit accounts and other Collateral Accounts, all certificates of deposit, fixtures, letters of credit rights (whether or not the letter of credit is evidenced by a writing), securities, and all other investment property, supporting obligations, and financial assets, whether now owned or hereafter acquired, wherever located; and

All Borrower's Books relating to the foregoing, and any and all claims, rights and interests in any of the above and all substitutions for, additions, attachments, accessories, accessions and improvements to and replacements, products, proceeds and insurance proceeds of any or all of the foregoing.

Notwithstanding the foregoing, the Collateral does not include any Intellectual Property, now owned or hereafter acquired; provided, however, the Collateral shall include all Accounts and all proceeds of Intellectual Property. If a judicial authority (including a U.S. Bankruptcy Court) would hold that a security interest in the underlying Intellectual Property is necessary to have a security interest in such Accounts and such property that are proceeds of Intellectual Property, then the Collateral shall automatically, and effective as of the Effective Date, include the Intellectual Property to the extent necessary to permit perfection of Collateral Agent's security interest in such Accounts and such other property of Borrower that are proceeds of the Intellectual Property; (ii) more than sixty-five percent (65%) of the total combined voting power of all classes of stock entitled to vote the shares of capital stock (the "Shares") of any Foreign Subsidiary, if Borrower demonstrates to Collateral Agent's reasonable satisfaction that a pledge of more than sixty-five percent (65%) of the Shares of such Subsidiary creates a present and existing adverse tax consequence to Borrower under the U.S. Internal Revenue Code; or (iii) any license or contract, in each case if the granting of a Lien in such license or contract or the enforcement of such Lien is prohibited by or would constitute a default under the agreement governing such license or contract (but (A) only to the extent such prohibition is enforceable under applicable law and (B) other than to the extent that any such term would be rendered ineffective pursuant to Sections 9-406, 9-408 or 9-409 (or any other Section) of Division 9 of the Code); provided that upon the termination, lapsing or expiration of any such prohibition, such license or contract, as applicable, shall automatically be subject to the security interest granted in favor of Collateral Agent hereunder and become part of the "Collateral."

Pursuant to the terms of the Loan and Security Agreement dated as of June 17, 2016 among Borrower, Collateral Agent, and the Lenders party thereto, Borrower has agreed not to encumber any of its Intellectual Property except as permitted thereby.

EXHIBIT B

Form of Disbursement Letter

[see attached]

DISBURSEMENT LETTER

[DATE]

The undersigned, being the duly elected and acting _____ of REGULUS THERAPEUTICS INC., a Delaware corporation with offices located at 10614 Science Center Dr., San Diego, California 92121 (“**Borrower**”), does hereby certify to **OXFORD FINANCE LLC** (“**Oxford**” and “**Lender**”), as collateral agent (the “**Collateral Agent**”) in connection with that certain Loan and Security Agreement dated as of June 17, 2016, by and among Borrower, Collateral Agent and the Lenders from time to time party thereto (the “**Loan Agreement**”; with other capitalized terms used below having the meanings ascribed thereto in the Loan Agreement) that:

1. The representations and warranties made by Borrower in Section 5 of the Loan Agreement and in the other Loan Documents are true and correct in all material respects as of the date hereof; provided, that those representations and warranties expressly referring to a specific date shall be true, accurate and complete in all material respects as of such date.

2. No event or condition has occurred that would constitute an Event of Default under the Loan Agreement or any other Loan Document.

3. Borrower is in compliance with the covenants and requirements contained in Sections 4, 6 and 7 of the Loan Agreement.

4. All conditions referred to in Section 3 of the Loan Agreement to the making of the Loan to be made on or about the date hereof have been satisfied or waived by Collateral Agent.

5. No Material Adverse Change has occurred.

6. The undersigned is a Responsible Officer.

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7. The proceeds of the Term [A][B] Loan shall be disbursed as follows:

Disbursement from Oxford:

Loan Amount	\$ _____
Plus:	
--Deposit Received	\$ _____
Less:	
--Facility Fee	(\$ _____)
[--Interim Interest	(\$ _____)]
--Lender's Legal Fees	(\$ _____)**

Net Proceeds due from Oxford: \$ _____

TOTAL TERM [A][B] LOAN NET PROCEEDS FROM LENDERS \$ _____

8. The [initial][Term Loan][Term A Loan] shall amortize in accordance with the Amortization Table attached hereto.

9. The aggregate net proceeds of the Term Loans shall be transferred to the Designated Deposit Account as follows:

Account Name:	<u>REGULUS THERAPEUTICS INC.</u>
Bank Name:	[_____]
Bank Address:	[_____]
Account Number:	_____
ABA Number:	[_____]

** Legal fees and costs are through the Effective Date. Post-closing legal fees and costs, payable after the Effective Date, to be invoiced and paid post-closing.

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Dated as of the date first set forth above.

BORROWER:

REGULUS THERAPEUTICS INC.

By

Name:

Title:

COLLATERAL AGENT AND LENDER:

OXFORD FINANCE LLC

By

Name:

Title:

[*Signature Page to Disbursement Letter*]

AMORTIZATION TABLE

(Term [A][B] Loan)

[see attached]

EXHIBIT C

Compliance Certificate

TO: OXFORD FINANCE LLC, as Collateral Agent and Lender

FROM: REGULUS THERAPEUTICS INC.

The undersigned authorized officer (“ **Officer** ”) of REGULUS THERAPEUTICS INC. (“ **Borrower** ”), hereby certifies that in accordance with the terms and conditions of the Loan and Security Agreement by and among Borrower, Collateral Agent, and the Lenders from time to time party thereto (the “ **Loan Agreement** ;” capitalized terms used but not otherwise defined herein shall have the meanings given them in the Loan Agreement),

(a) Borrower is in complete compliance for the period ending _____ with all required covenants in the Loan Agreement except as noted below;

(b) There are no Events of Default, except as noted below;

(c) Except as noted below, all representations and warranties of Borrower stated in the Loan Documents are true and correct in all material respects on this date and for the period described in (a), above; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true, accurate and complete in all material respects as of such date.

(d) Borrower, and each of Borrower’s Subsidiaries, has timely filed all required tax returns and reports or extensions therefor, Borrower, and each of Borrower’s Subsidiaries, has timely paid all foreign, federal, state, and local taxes, assessments, deposits and contributions owed by Borrower, or Subsidiary, except as otherwise permitted pursuant to the terms of Section 5.8 of the Loan Agreement;

(e) No Liens have been levied or claims made against Borrower or any of its Subsidiaries relating to unpaid employee payroll or benefits of which Borrower has not previously provided written notification to Collateral Agent and the Lenders.

Attached are the required documents, if any, supporting our certification(s). The Officer, on behalf of Borrower, further certifies that the attached financial statements are prepared in accordance with Generally Accepted Accounting Principles (GAAP) and are consistently applied from one period to the next except as explained in an accompanying letter or footnotes and except, in the case of unaudited financial statements, for the absence of footnotes and subject to year-end audit adjustments as to the interim financial statements.

Please indicate compliance status since the last Compliance Certificate by circling Yes, No, or N/A under "Complies" column.

	Reporting Covenant	Requirement	Actual	Complies		
1)	Financial statements - balance sheet and income statement	Monthly within 30 days		Yes	No	N/A
2)	Financial statements - cash flow statement	Quarterly within 45 days		Yes	No	N/A
3)	Annual (CPA Audited) statements	Within 120 days after FYE		Yes	No	N/A
4)	Annual Financial Projections/Budget (prepared on a monthly basis)	Annually (within 45 days of FYE), and when revised		Yes	No	N/A
5)	8-K, 10-K and 10-Q Filings	If applicable, within 5 days of filing		Yes	No	N/A
6)	Compliance Certificate	Monthly within 30 days		Yes	No	N/A
7)	IP Report	When required		Yes	No	N/A
8)	Total amount of Borrower's cash and cash equivalents at the last day of the measurement period		\$ _____	Yes	No	N/A
9)	Total amount of Borrower's Subsidiaries' cash and cash equivalents at the last day of the measurement period		\$ _____	Yes	No	N/A

Deposit and Securities Accounts

(Please list all accounts; attach separate sheet if additional space needed)

	Institution Name	Account Number	New Account?		Account Control Agreement in place?	
1)			Yes	No	Yes	No
2)			Yes	No	Yes	No
3)			Yes	No	Yes	No
4)			Yes	No	Yes	No

Other Matters

- | | | | |
|----|--|-----|----|
| 1) | Have there been any changes in management since the last Compliance Certificate? | Yes | No |
| 2) | Have there been any transfers/sales/disposals/retirement of Collateral or IP prohibited by the Loan Agreement? | Yes | No |
| 3) | Have there been any new or pending claims or causes of action against Borrower that involve more than Two Hundred Fifty Thousand Dollars (\$250,000.00)? | Yes | No |
| 4) | Have there been any amendments of or other changes to the Borrower's Operating Documents or any of its Subsidiaries' Operating Documents? If the Borrower is no longer subject to Securities Exchange Act of 1934, as amended, have there been any material changes to the capitalization of Borrower? If yes, please provide copies of any such amendments or changes to the Operating Documents and capitalization table, as applicable, with this Compliance Certificate. | Yes | No |
-

Exceptions

Please explain any exceptions with respect to the certification above: (If no exceptions exist, state "No exceptions." Attach separate sheet if additional space needed.)

REGULUS THERAPEUTICS INC.

By _____
Name: _____
Title: _____

Date:

LENDER USE ONLY

Received by: _____ Date: _____
Verified by: _____ Date: _____
Compliance Status: Yes No

EXHIBIT D

Form of Secured Promissory Note

[see attached]

SECURED PROMISSORY NOTE

(Term [A][B] Loan)

\$ _____

Dated: [DATE]

FOR VALUE RECEIVED, the undersigned, REGULUS THERAPEUTICS INC., a Delaware corporation with offices located at 10614 Science Center Dr., San Diego, California 92121 (“**Borrower**”) HEREBY PROMISES TO PAY to the order of OXFORD FINANCE LLC (“**Lender**”) the principal amount of [] MILLION DOLLARS (\$ _____) or such lesser amount as shall equal the outstanding principal balance of the Term [A][B] Loan made to Borrower by Lender, plus interest on the aggregate unpaid principal amount of such Term [A][B] Loan, at the rates and in accordance with the terms of the Loan and Security Agreement dated June 17, 2016 by and among Borrower, Lender, Oxford Finance LLC, as Collateral Agent, and the other Lenders from time to time party thereto (as amended, restated, supplemented or otherwise modified from time to time, the “**Loan Agreement**”). If not sooner paid, the entire principal amount and all accrued and unpaid interest hereunder shall be due and payable on the Maturity Date as set forth in the Loan Agreement. Any capitalized term not otherwise defined herein shall have the meaning attributed to such term in the Loan Agreement.

Principal, interest and all other amounts due with respect to the Term [A][B] Loan, are payable in lawful money of the United States of America to Lender as set forth in the Loan Agreement and this Secured Promissory Note (this “**Note**”). The principal amount of this Note and the interest rate applicable thereto, and all payments made with respect thereto, shall be recorded by Lender and, prior to any transfer hereof, endorsed on the grid attached hereto which is part of this Note.

The Loan Agreement, among other things, (a) provides for the making of a secured Term [A][B] Loan by Lender to Borrower, and (b) contains provisions for acceleration of the maturity hereof upon the happening of certain stated events.

This Note may not be prepaid except as set forth in Section 2.2 (c) and Section 2.2(d) of the Loan Agreement.

This Note and the obligation of Borrower to repay the unpaid principal amount of the Term [A][B] Loan, interest on the Term [A][B] Loan and all other amounts due Lender under the Loan Agreement is secured under the Loan Agreement.

Presentment for payment, demand, notice of protest and all other demands and notices of any kind in connection with the execution, delivery, performance and enforcement of this Note are hereby waived.

Borrower shall pay all reasonable fees and expenses, including, without limitation, reasonable attorneys’ fees and costs, incurred by Lender in the enforcement or attempt to enforce any of Borrower’s obligations hereunder not performed when due.

This Note shall be governed by, and construed and interpreted in accordance with, the internal laws of the State of California.

The ownership of an interest in this Note shall be registered on a record of ownership maintained by Lender or its agent. Notwithstanding anything else in this Note to the contrary, the right to the principal of, and stated interest on, this Note may be transferred only if the transfer is registered on such record of ownership and the transferee is identified as the owner of an interest in the obligation. Borrower shall be entitled to treat the registered holder of this Note (as recorded on such record of ownership) as the owner in fact thereof for all purposes and shall not be bound to recognize any equitable or other claim to or interest in this Note on the part of any other person or entity.

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IN WITNESS WHEREOF, Borrower has caused this Note to be duly executed by one of its officers thereunto duly authorized on the date hereof.

BORROWER:

REGULUS THERAPEUTICS INC.

By: _____

Name: _____

Title: _____

LOAN INTEREST RATE AND PAYMENTS OF PRINCIPAL

<u>Date</u>	<u>Principal Amount</u>	<u>Interest Rate</u>	<u>Scheduled Payment Amount</u>	<u>Notation By</u>
-------------	-----------------------------	----------------------	-------------------------------------	--------------------

CORPORATE BORROWING CERTIFICATE

Borrower: REGULUS THERAPEUTICS INC.

Date : [DATE]

Lender: OXFORD FINANCE LLC, as Collateral Agent and Lender

I hereby certify as follows, as of the date set forth above:

1. I am the Secretary, Assistant Secretary or other officer of Borrower. My title is as set forth below.
2. Borrower's exact legal name is set forth above. Borrower is a corporation existing under the laws of the State of Delaware.
3. Attached hereto as Exhibit A and Exhibit B, respectively, are true, correct and complete copies of (i) Borrower's Articles/Certificate of Incorporation (including amendments), as filed with the Secretary of State of the state in which Borrower is incorporated as set forth in paragraph 2 above; and (ii) Borrower's Bylaws. Neither such Articles/Certificate of Incorporation nor such Bylaws have been amended, annulled, rescinded, revoked or supplemented, and such Articles/Certificate of Incorporation and such Bylaws remain in full force and effect as of the date hereof.
4. The following resolutions were duly and validly adopted by Borrower's Board of Directors at a duly held meeting of such directors (or pursuant to a unanimous written consent or other authorized corporate action). Such resolutions are in full force and effect as of the date hereof and have not been in any way modified, repealed, rescinded, amended or revoked, and the Lenders may rely on them until each Lender receives written notice of revocation from Borrower.

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Resolved , that **any one** of the following officers or employees of Borrower, whose names, titles and signatures are below, may act on behalf of Borrower:

<u>Name</u>	<u>Title</u>	<u>Signature</u>	Authorized to Add or Remove <u>Signatories</u>
_____	_____	_____	<input type="checkbox"/>
_____	_____	_____	<input type="checkbox"/>
_____	_____	_____	<input type="checkbox"/>
_____	_____	_____	<input type="checkbox"/>

Resolved Further, that **any one** of the persons designated above with a checked box beside his or her name may, from time to time, add or remove any individuals to and from the above list of persons authorized to act on behalf of Borrower.

Resolved Further, that such individuals may, on behalf of Borrower:

Borrow Money . Borrow money from the Lenders.

Execute Loan Documents . Execute any loan documents any Lender requires.

Grant Security . Grant Collateral Agent a security interest in any of Borrower's assets.

Negotiate Items . Negotiate or discount all drafts, trade acceptances, promissory notes, or other indebtedness in which Borrower has an interest and receive cash or otherwise use the proceeds.

Further Acts . Designate other individuals to request advances, pay fees and costs and execute other documents or agreements (including documents or agreement that waive Borrower's right to a jury trial) they believe to be necessary to effectuate such resolutions.

Resolved Further, that all acts authorized by the above resolutions and any prior acts relating thereto are ratified.

[Balance of Page Intentionally Left Blank]

5. The persons listed above are Borrower's officers or employees with their titles and signatures shown next to their names.

By: _____

Name: _____

Title: _____

**** If the Secretary, Assistant Secretary or other certifying officer executing above is designated by the resolutions set forth in paragraph 4 as one of the authorized signing officers, this Certificate must also be signed by a second authorized officer or director of Borrower.*

I, the _____ of Borrower, hereby certify as to paragraphs 1 through 5 above, as
[print title]
of the date set forth above.

By: _____

Name: _____

Title: _____

[*Signature Page to Corporate Borrowing Certificate*]

EXHIBIT A

Articles/Certificate of Incorporation (including amendments)

[see attached]

EXHIBIT B

Bylaws

[see attached]

DEBTOR: REGULUS THERAPEUTICS INC.
SECURED PARTY: OXFORD FINANCE LLC,
as Collateral Agent

EXHIBIT A TO UCC FINANCING STATEMENT

Description of Collateral

The Collateral consists of all of Debtor's right, title and interest in and to the following personal property:

All goods, Accounts (including health-care receivables), Equipment, Inventory, contract rights or rights to payment of money, leases, license agreements, franchise agreements, General Intangibles (except as noted below), commercial tort claims, documents, instruments (including any promissory notes), chattel paper (whether tangible or electronic), cash, deposit accounts and other Collateral Accounts, all certificates of deposit, fixtures, letters of credit rights (whether or not the letter of credit is evidenced by a writing), securities, and all other investment property, supporting obligations, and financial assets, whether now owned or hereafter acquired, wherever located; and

All Debtor's Books relating to the foregoing, and any and all claims, rights and interests in any of the above and all substitutions for, additions, attachments, accessories, accessions and improvements to and replacements, products, proceeds and insurance proceeds of any or all of the foregoing.

Notwithstanding the foregoing, the Collateral does not include (i) any Intellectual Property, now owned or hereafter acquired; provided, however, the Collateral shall include all Accounts and all proceeds of Intellectual Property. If a judicial authority (including a U.S. Bankruptcy Court) would hold that a security interest in the underlying Intellectual Property is necessary to have a security interest in such Accounts and such property that are proceeds of Intellectual Property, then the Collateral shall automatically, and effective as of the Effective Date, include the Intellectual Property to the extent necessary to permit perfection of Collateral Agent's security interest in such Accounts and such other property of Debtor that are proceeds of the Intellectual Property; (ii) more than sixty-five percent (65%) of the total combined voting power of all classes of stock entitled to vote the shares of capital stock (the "Shares") of any Foreign Subsidiary, if Debtor demonstrates to Collateral Agent's reasonable satisfaction that a pledge of more than sixty-five percent (65%) of the Shares of such Subsidiary creates a present and existing adverse tax consequence to Debtor under the U.S. Internal Revenue Code; or (iii) any license or contract, in each case if the granting of a Lien in such license or contract or the enforcement of such Lien is prohibited by or would constitute a default under the agreement governing such license or contract (but (A) only to the extent such prohibition is enforceable under applicable law and (B) other than to the extent that any such term would be rendered ineffective pursuant to Sections 9-406, 9-408 or 9-409 (or any other Section) of Division 9 of the Code); provided that upon the termination, lapsing or expiration of any such prohibition, such license or contract, as applicable, shall automatically be subject to the security interest granted in favor of Collateral Agent hereunder and become part of the "Collateral."

Pursuant to the terms of the Loan and Security Agreement dated as of June 17, 2016 among Debtor, Collateral Agent, and the Lenders party thereto, Debtor has agreed not to encumber any of its Intellectual Property except as permitted thereby.

Capitalized terms used but not defined herein have the meanings ascribed in the Uniform Commercial Code in effect in the State of California as in effect from time to time (the "Code") or, if not defined in the Code, then in the Loan and Security Agreement by and between Debtor, Secured Party and the other Lenders party thereto (as modified, amended and/or restated from time to time).

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Paul C. Grint, M.D., certify that:

1. I have reviewed this quarterly report on Form 10-Q of Regulus Therapeutics Inc.;
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 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 13(a)-15(f) and 15(d)-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 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 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 functions):
 - 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.

Date: August 2, 2016

/s/ Paul C. Grint

Paul C. Grint, M.D.

President and Chief Executive Officer

(Principal Executive Officer)

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Joseph P. Hagan, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Regulus Therapeutics Inc.;
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 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 13(a)-15(f) and 15(d)-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 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 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 functions):
 - 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.

Date: August 2, 2016

/s/ Joseph P. Hagan

Joseph P. Hagan

Chief Operating Officer

(Principal Financial and Accounting Officer)

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 Regulus Therapeutics Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Paul C. Grint, M.D., President and Chief Executive Officer and I, Joseph P. Hagan, Chief Operating Officer and Principal Financial and Accounting Officer, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 2, 2016

/s/ Paul C. Grint

Paul C. Grint, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: August 2, 2016

/s/ Joseph P. Hagan

Joseph P. Hagan
Chief Operating Officer
(Principal Financial and Accounting Officer)

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document.