UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 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 001-36395

CERULEAN PHARMA INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**20-4139823**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
35 Gatehouse Drive Waltham, MA	**02451**
(Address of Principal Executive Offices)	**(Zip Code)**

(781) 996-4300
(Registrant's Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

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 the 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. (Check one):

Large accelerated filer	☐		Accelerated filer	☒
Non-accelerated filer	☐	(Do not check if a smaller reporting company)	Smaller reporting company	☐

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

Number of shares of the registrant's Common Stock, $ 0.0001 par value, outstanding on August 1, 2016: 27,384,492

CERULEAN PHARMA INC.

FORM 10-Q
FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2016

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements.

CERULEAN PHARMA INC.

CONDENSED CONSOLIDATED BALANCE SHEETS (unaudited)
(in thousands except share data and par value)

	June 30, 2016	December 31, 2015
ASSETS		
Current assets:		
Cash and cash equivalents	$ 47,193	$ 75,908
Accounts receivable, prepaid expenses, and other current assets	1,729	1,394
Total current assets	48,922	77,302
Property and equipment, net	740	576
Other assets	230	347
Total	$ 49,892	$ 78,225
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Current portion of loan payable	$ 8,017	$ 7,652
Accounts payable	1,593	2,226
Accrued expenses	4,852	6,459
Total current liabilities	14,462	16,337
Long-term liabilities:		
Loan payable, net of current portion	8,649	12,672
Other long-term liabilities	941	473
Total long-term liabilities	9,590	13,145
Commitments and contingencies		
Stockholders' equity:		
Preferred stock $0.01 par value; 5,000,000 shares authorized, no shares issued or outstanding	—	—
Common stock, $0.0001 par value; 120,000,000 shares authorized, 27,363,965 and 27,346,780 shares issued and outstanding at June 30, 2016 and December 31, 2015, respectively	3	3
Additional paid-in capital	211,613	210,115
Accumulated deficit	(185,776)	(161,375)
Total stockholders' equity	25,840	48,743
Total	$ 49,892	$ 78,225

See notes to unaudited condensed consolidated financial statements.

CERULEAN PHARMA INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS (unaudited)
(in thousands except per share and share data)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Revenue	$ —	$ —	$ —	$ -
Operating expenses:				
Research and development	7,522	6,678	17,292	11,699
General and administrative	2,773	2,717	5,891	5,398
Total operating expenses	10,295	9,395	23,183	17,097
Other income (expense):				
Interest income	25	1	41	4
Interest expense	(597)	(513)	(1,260)	(1,234)
Other income (expense)	8	—	1	(8)
Total other expense, net	(564)	(512)	(1,218)	(1,238)
Net loss attributable to common stockholders	$ (10,859)	$ (9,907)	$ (24,401)	$ (18,335)
Net loss per share attributable to common stockholders:				
Basic and diluted	$ (0.40)	$ (0.37)	$ (0.89)	$ (0.78)
Weighted-average common shares outstanding:				
Basic and diluted	27,363,965	26,690,673	27,363,304	23,504,303

See notes to unaudited condensed consolidated financial statements.

CERULEAN PHARMA INC.

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

	Six Months Ended June 30,	
	2016	**2015**
Cash flows from operating activities:		
Net loss	$ (24,401)	$ (18,335)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	1,457	896
Noncash rent expense	134	(13)
Depreciation and amortization	127	83
Amortization of debt discount and deferred financing costs	242	791
Loss on disposal of property and equipment	4	—
Changes in operating assets and liabilities:		
Accounts receivable, prepaid expenses and other current assets	(334)	532
Accounts payable	(458)	503
Accrued expenses	(1,272)	(195)
Net cash used in operating activities	(24,501)	(15,738)
Cash flows from investing activities:		
Purchases of property and equipment	(472)	(107)
Decrease (increase) in restricted cash	117	(230)
Net cash used in investing activities	(355)	(337)
Cash flows from financing activities:		
Proceeds from sale of common stock	41	2,472
Proceeds from public stock offering, net of issuance costs	—	37,185
Proceeds from issuance of loans payable	—	15,000
Payments on loans payable	(3,900)	(3,921)
Cash paid for debt issuance costs	—	(359)
Net cash (used in) provided by financing activities	(3,859)	50,377
Net (decrease) increase in cash and cash equivalents	(28,715)	34,302
Cash and cash equivalents — Beginning of period	75,908	51,174
Cash and cash equivalents — End of period	$ 47,193	$ 85,476
Supplemental cash flow information — Interest paid	$ 708	$ 443

See notes to the unaudited condensed consolidated financial statements.

CERULEAN PHARMA INC.

NOTES TO UNAUDITED CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

1. NATURE OF BUSINESS AND OPERATIONS

Nature of Business — Cerulean Pharma Inc. (the "Company") was incorporated on November 28, 2005, as a Delaware corporation and is located in Waltham, Massachusetts. The Company was formed to develop novel, nanotechnology-based therapeutics in the areas of oncology and other diseases.

Basis of Presentation — The condensed consolidated financial statements include the accounts of the Company and its subsidiary, Cerulean Pharma Australia Pty Ltd, a wholly owned Australian-based proprietary limited company. All intercompany accounts and transactions have been eliminated. The consolidated interim financial statements of the Company included herein have been prepared, without audit, pursuant to the rules and regulations of the Securities and Exchange Commission (the "SEC"). Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States of America have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these condensed consolidated financial statements should be read in conjunction with the Company's audited financial statements as of and for the year ended December 31, 2015, and notes thereto, included in the Company's Annual Report on Form 10-K, which was filed with the SEC on March 10, 2016 (the "2015 10-K").

The unaudited condensed consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements. In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments that are necessary to present fairly the Company's financial position as of June 30, 2016 and the results of its operations for the three and six months ended June 30, 2016 and 2015 and cash flows for the six months ended June 30, 2016 and 2015. Such adjustments are of a normal and recurring nature. The results for the three and six months ended June 30, 2016, are not indicative of the results for the year ending December 31, 2016, or for any future period.

As a clinical stage entity, the Company has incurred historical operating losses resulting in an accumulated deficit of $185.8 million at June 30, 2016. The Company expects to continue to incur significant expenses and increasing operating losses for at least several years. To date, the Company has financed its operations primarily through private placements of its preferred stock, proceeds from borrowings, an initial public offering completed in 2014 and a follow-on offering completed in 2015. The Company has not completed development of any product candidate and has devoted substantially all of its financial resources and efforts to research and development, including preclinical and clinical development. Accordingly, the Company will continue to depend on its ability to raise capital through equity and debt issuances and/or through strategic partnerships. The Company believes its cash and cash equivalents of approximately $47.2 million at June 30, 2016, are sufficient to fund its planned operations into the second quarter of 2017 and it has the ability to reduce or defer operating expenses as may be needed to fund its operations into the third quarter of 2017. The Company will need to raise additional capital to continue to fund its long-term operations. Should its operating plan change further, or prove to be inaccurate, then the Company will be required to reassess its operating capital needs. However, there can be no assurance that the Company will have the cash resources to fund its operating plan or that additional funding will be available on terms acceptable to it, or at all.

2. SIGNIFICANT ACCOUNTING POLICIES

There have been no material changes to the significant accounting policies previously disclosed in the 2015 10-K.

Recent Accounting Pronouncements – In March 2016, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update 2016-09, "Improvements to Employee Share-Based Payment Accounting" ("ASU 2016-09"). ASU 2016-09 is intended to simplify various aspects of how share-based payments are accounted for and presented in financial statements. The standard is effective prospectively for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2016, with early adoption permitted. The Company is currently evaluating the effect this standard will have on its consolidated financial statements and related disclosures.

In February 2016, the FASB issued Accounting Standards Update 2016-02, "Leases" ("ASU 2016-02"), which provides new accounting guidance on leases. ASU 2016-02 requires lessees to recognize leases on their balance sheets, and leaves lessor accounting largely unchanged. The amendments in ASU 2016-02 are effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early application is permitted for all entities. ASU 2016-02 requires a modified retrospective approach for all leases existing at, or entered into after, the date of initial application, with an option to elect to use certain transition relief. The Company is currently evaluating the impact of this new standard on its consolidated financial statements and related disclosures.

In August 2014, the FASB issued Accounting Standards Update 2014-15, "Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern" ("ASU 2014-15"). ASU 2014-15 requires management to evaluate, at each annual and interim reporting period, whether there are conditions or events that raise substantial doubt about the entity's ability to continue as a going concern and provide related disclosures. ASU 2014-15 is effective for annual and interim reporting periods beginning January 1, 2017 and is not expected to have a material impact on the Company's consolidated financial statements.

3. NET LOSS PER SHARE ATTRIBUTABLE TO COMMON STOCKHOLDERS

The Company computes diluted loss per common share after giving effect to the dilutive effect of stock options, warrants and shares of unvested restricted stock that are outstanding during the period, except where the inclusion of such securities would be antidilutive.

The Company has reported a net loss for all periods presented and, therefore, diluted net loss per common share is the same as basic net loss per common share.

The following potentially dilutive securities that were outstanding prior to the use of the treasury stock method have been excluded from the computation of diluted weighted-average shares outstanding, because the inclusion of such securities would have an antidilutive impact due to the losses reported (in common stock equivalent shares):

	As of June 30,	
	2016	2015
Options to purchase common stock	4,145,988	2,989,627
Warrants to purchase common stock	300,564	300,564

4. ACCRUED EXPENSES

Accrued expenses consist of the following (in thousands):

	As of June 30, 2016	As of December 31, 2015
Accrued clinical trial costs	$ 1,789	$ 2,631
Accrued contract manufacturing expenses	1,016	945
Accrued compensation and benefits	1,234	1,864
Accrued interest	104	136
Other accrued expenses	709	883
Total accrued expenses	$ 4,852	$ 6,459

5. LOAN AGREEMENTS

On January 8, 2015, the Company entered into a loan and security agreement with Hercules Technology Growth Capital, Inc. ("Hercules") to borrow up to $26.0 million (the "Hercules Loan Agreement"). The proceeds were used to repay the Company's then-existing term loan facility with Lighthouse Capital Partners VI, L.P. ("Lighthouse Capital") and for general corporate and working capital purposes. At June 30, 2016 and December 31, 2015, the Company had $17.1 million and $21.0 million, respectively, outstanding under the Hercules Loan Agreement.

The Hercules Loan Agreement will mature on July 1, 2018. Each advance under the Hercules Loan Agreement accrues interest at a floating per annum rate equal to the greater of (i) 7.30% or (ii) the sum of 7.30% plus the prime rate minus 5.75%. The Hercules Loan Agreement provided for interest-only payments on a monthly basis until December 31, 2015. Thereafter, payments are payable monthly in equal installments of principal and interest to fully amortize the outstanding principal over the remaining term of the loan, subject to recalculation upon a change in the prime rate. Failure to make payments or comply with other covenants as stated in the Hercules Loan Agreement could result in an event of default and acceleration of amounts due. In such case, the Company may not be able to make accelerated payments, and Hercules could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all of the Company's assets other than its intellectual property. At the end of the loan term (whether at maturity, by prepayment in full or otherwise), the Company shall pay a final end of term charge to Hercules in the amount of 6.7% of the aggregate original principal amount advanced by Hercules. The amount of the end of term charge is being accrued over the loan term as interest expense.

In connection with the Hercules Loan Agreement, the Company issued to Hercules a warrant to purchase shares of the common stock of the Company at an exercise price of $6.05 per share. The warrant is exercisable for 171,901 shares of common stock. The warrant is exercisable until January 8, 2020. The Company estimated the fair value of the warrant for shares exercisable on the issue

date in January 2015 to be $824,000. The value of the warrant was recorded as a discount to the loan and will be amortized to interest expense using the effective interest method over the term of the loan.

In December 2011, the Company entered into a loan and security agreement with Lighthouse Capital to borrow up to $10.0 million in one or more advances by December 31, 2012. In both March 2012 and August 2012, the Company borrowed $5.0 million under the loan and security agreement, for a total of $10.0 million. This amount was being repaid over 36 months beginning on December 1, 2012, at an interest rate of 8.25%. In addition, the Company was required to make an additional payment in the amount of $600,000 at the end of the loan term. The amount was accrued over the loan term as interest expense. In January 2015, the Company repaid in full the amount outstanding under the Lighthouse Capital loan, or $3.6 million, with the proceeds from the Hercules Loan Agreement.

In connection with the loan and security agreement with Lighthouse Capital, the Company issued Lighthouse Capital a warrant to purchase a maximum of 66,436 shares of the Company's Series D Preferred Stock, at an exercise price of $12.04 per share and with an expiration date 10 years from the date of issue (December 2021). The Company determined the fair value of the warrant at the end of each reporting period using the Black-Scholes option pricing model until the warrant converted to a warrant to purchase 66,436 shares of common stock upon the completion of the Company's initial public offering. The value of the warrant was recorded as a discount to the loan and was being amortized as interest expense using the effective interest method over the 36-month repayment term. The unamortized discount relating to the warrants, or $0.2 million, was expensed as interest expense upon repayment of the loan in January 2015.

6. STOCK-BASED COMPENSATION

In March 2014, the Company's board of directors adopted and its stockholders approved the 2014 Stock Incentive Plan (the "2014 Plan") and the 2014 Employee Stock Purchase Plan (the "ESPP"), which became effective in April 2014.

Stock Options

The 2014 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. A summary of stock option activity for employee, director and nonemployee awards under all stock option plans during the six months ended June 30, 2016 is presented below (Aggregate Intrinsic Value in thousands):

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value
Outstanding — January 1, 2016	3,454,926	$ 5.39	8.9	$ —
Granted	707,070	$ 2.78		
Exercised	—	—		
Forfeited	(16,008)	$ 4.46		
Outstanding — June 30, 2016	4,145,988	$ 4.95	8.6	$ 7
Options expected to vest — June 30, 2016	2,619,425	$ 4.57	9.1	$ 7
Options exercisable — June 30, 2016	1,394,581	$ 5.68	7.6	$ —

The weighted-average per share grant date fair value of options granted during the six months ended June 30, 2016 and 2015 was $1.31 and $2.44, respectively.

The fair value of each option award is estimated on the date of grant using the Black-Scholes option-pricing model based on the assumptions noted in the table below. Expected volatility for the Company's common stock was determined based on an average of the historical volatility of a peer-group of similar public companies. The Company has limited option exercise information, and as such, the expected term of the options granted was calculated using the simplified method that represents the average of the contractual term of the option and the weighted-average vesting period of the option. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate for periods within the contractual life of the option is based upon the U.S. Treasury yield curve in effect at the time of grant.

The Company has recorded stock-based compensation expense related to the issuance of stock option awards to employees of $690,000 and $403,000 for the three months ended June 30, 2016 and 2015, respectively, and $1.4 million and $823,000 for the six months ended June 30, 2016 and 2015, respectively. The assumptions used in the Black-Scholes option-pricing model for stock

options granted to employees and to directors in respect of board services during the three and six months ended June 30, 2016 and 2015 are as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Expected life	5.5 years	5.4-6.1 years	5.5-6.1 years	5.4-6.1 years
Risk-free interest rate	1.2%	1.8%-2.0%	1.2%-1.9%	1.5%-2.0%
Expected volatility	61%	61%	61%	61%-63%
Expected dividend rate	—%	—%	—%	—%

The Company recorded stock-based compensation expense related to nonemployee awards of $14,000 and $53,000 for the three months ended June 30, 2016 and 2015, respectively and $52,000 and $73,000 for the six months ended June 30, 2016 and 2015, respectively. The compensation expense related to nonemployee awards is included in the total stock-based compensation each year and is subject to re-measurement until the options vest. The fair value of the grants is being expensed over the vesting period of the options on a straight-line basis as the services are being provided. The Black-Scholes assumptions used to estimate fair value for the three and six months ended June 30, 2016 and 2015 were as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Expected life	9.0-9.6 years	10 years	6.9-9.7 years	10 years
Risk-free interest rate	1.7%-2.0%	2.2%-2.3%	1.7%-2.0%	2.2%-2.3%
Expected volatility	61%	59%	60%-61%	59%
Expected dividend rate	—%	—%	—%	—%

There were no nonemployee stock option awards granted during the six months ended June 30, 2016. During the six months ended June 30, 2015, the Company granted nonemployee stock options to purchase 180,000 shares of the Company's common stock. The weighted-average exercise price and the weighted-average grant date fair value of nonemployee stock options granted for the six months ended June 30, 2015 was $5.30 per share and $3.07 per share, respectively.

Employee Stock Purchase Plan

The ESPP permits eligible employees to enroll in a six-month offering period whereby participants may purchase shares of the Company's common stock, through payroll deductions, at a price equal to 85% of the closing price of the common stock on the first day of the offering period or the last day of the offering period, whichever is lower. Purchase dates under the ESPP occur on or about June 30 and December 31 of each year. The first offering period under the ESPP opened on July 1, 2015. During the six months ended June 30, 2016, 17,185 shares of common stock were purchased under the ESPP at a price of $2.38 per share. The stock-based compensation expense related to the ESPP for the three and six months ended June 30, 2016 was $12,000 and $24,000, respectively. There was no stock-based compensation related to the ESPP recorded for the three and six months ended June 30, 2015.

7. FAIR VALUE MEASUREMENTS

The Company's financial instruments consist of cash equivalents, accounts payable, accrued expenses, and debt obligations. The carrying amount of accounts payable and accrued expenses are considered a reasonable estimate of their fair value, due to the short-term maturity of these instruments. The carrying amount of debt is also considered to be a reasonable estimate of its fair value based on the short term nature of the debt and because the debt bears interest at the prevailing market rate for instruments with similar characteristics.

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value are performed in a manner to maximize the use of observable inputs and minimize the use of unobservable inputs.

The accounting standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value, which are the following:

Level 1 — Quoted prices (unadjusted) in active markets that are accessible at the market date for identical unrestricted assets or liabilities.

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

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

A summary of the financial assets and liabilities that are measured on a recurring basis at fair value as of June 30, 2016 and December 31, 2015, is as follows (in thousands):

		Fair Value Measurements Using		
	Carrying Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
June 30, 2016				
Money market funds	$ 46,616	$ —	$ 46,616	$ —
December 31, 2015				
Money market funds	$ 75,325	$ —	$ 75,325	$ —

The Company believes that its debt obligations bear interest at rates which approximate prevailing market rates for instruments with similar characteristics and, accordingly, the carrying values for these instruments approximate fair value. The Company's debt obligations are Level 2 measurements in the fair value hierarchy.

The Company's money market funds have been valued on the basis of valuations provided by third-party pricing services, as derived from such services' pricing models. Inputs to the models may include, but are not limited to, reported trades, executable bid and asked prices, broker/dealer quotations, prices or yields of securities with similar characteristics, benchmark curves or information pertaining to the issuer, as well as industry and economic events. The pricing services may use a matrix approach, which considers information regarding securities with similar characteristics to determine the valuation for a security. The Company is ultimately responsible for the consolidated financial statements and underlying estimates. Accordingly, the Company assesses the reasonableness of the valuations provided by the third-party pricing services by reviewing actual trade data, broker/dealer quotes and other similar data, which are obtained from quoted market prices or other sources.

No transfers between levels occurred during the periods presented.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our condensed consolidated financial statements and the related notes appearing elsewhere in this Quarterly Report on Form 10-Q. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section of this Quarterly Report on Form 10-Q for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage, oncology-focused company applying our proprietary Dynamic Tumor Targeting™ Platform to develop differentiated therapies. We were incorporated under the laws of the State of Delaware on November 28, 2005, under the name Tempo Pharmaceuticals, Inc. In October 2008, we changed our name to Cerulean Pharma Inc.

Our Dynamic Tumor Targeting Platform is designed to create nanoparticle-drug conjugates, or NDCs, with the aim of providing safer and more effective therapies for patients living with cancer. NDCs consist of anti-cancer therapeutics, or payloads, covalently linked to a proprietary polymer. We believe our NDCs concentrate their anti-cancer payloads inside tumor cells while sparing normal tissue because they are small enough to pass through the leaky pores of new blood vessels in tumors as an entry portal into tumor tissue, but are too large to pass through the pores of healthy blood vessels. Once inside tumors, we believe our NDCs are actively taken up into tumor cells where they slowly release their anti-cancer payloads, providing a durable inhibition of their targets.

We believe that the ability to combine our NDCs with other agents, either approved or experimental, is a key differentiating feature of our platform. Based on their properties and design, our NDCs have the potential to enable synergistic combination therapies that can offer better tolerability and efficacy. We believe that better tolerability can be achieved through the preferential accumulation of the NDC in the tumor cells while better efficacy can be achieved by combining drugs that have different and complementary mechanisms of action.

Our platform has generated two clinical-stage NDCs. Our first platform-generated clinical candidate, CRLX101, is in Phase 2 clinical development in patients with relapsed renal cell carcinoma, or RCC, and in relapsed ovarian cancer, and in other earlier stage clinical trials. In April 2015, the United States Food and Drug Administration, or FDA, granted CRLX101 fast track designation in combination with Avastin in metastatic RCC, and in July 2016 the FDA granted CRLX101 fast track designation in combination with paclitaxel for the treatment of platinum-resistant ovarian carcinoma, fallopian tube or primary peritoneal cancer. In May 2015, the FDA also granted CRLX101 orphan drug designation for the treatment of ovarian cancer. Our second platform-generated clinical candidate, CRLX301, is currently in Phase 1/2a clinical development. We intend to generate additional candidates, alone and potentially in collaboration with partners.

We are pursuing development of CRLX101 in combination with anti-cancer therapies in multiple ongoing clinical development programs that include company-sponsored trials and investigator-sponsored trials, or ISTs. Our two lead indications are relapsed RCC and relapsed ovarian cancer. In relapsed RCC, we are conducting a Phase 2 randomized, controlled, company-sponsored trial comparing CRLX101 administered in combination with Avastin to investigator's choice of standard of care in patients with RCC who have received two or three prior lines of therapy. We refer to this trial as the RCC Trial. We completed enrollment in October 2015 and expect to announce top-line data from the RCC Trial in the third quarter of 2016. In July 2016, we decided to amend the primary endpoint of the RCC Trial, so that progression free survival, or PFS, is assessed by independent radiologic review. Before this amendment, the primary endpoint of the RCC Trial was PFS as assessed by investigators, according to Response Evaluation Criteria In Solid Tumors, or RECIST, version 1.1. The amendment makes investigator-assessed PFS a secondary endpoint.

We have two ongoing trials in relapsed ovarian cancer. We are conducting a Phase 1b/2 company-sponsored trial of CRLX101 in combination with weekly paclitaxel in patients with relapsed ovarian cancer in collaboration with the GOG Foundation, Inc. (formerly known as the Gynecologic Oncology Group), or GOG. This Phase 1b/2 multi-center, open-label study combines CRLX101 with weekly paclitaxel in approximately 40 patients with recurrent or persistent epithelial ovarian, fallopian tube or primary peritoneal cancer. The Phase 1b portion of this clinical trial was designed to identify the maximum tolerated dose, or MTD, as well as pharmacokinetics, safety, tolerability and preliminary signals of efficacy of CRLX101 in combination with weekly paclitaxel. In April 2016, we announced the determination of the MTD and recommended Phase 2 dose for this combination to be 15 mg/m2 for CRLX101 administered every other week and 80 mg/m2 for weekly paclitaxel administered three weeks on and one week off. The Phase 2 expansion portion of this clinical trial is ongoing and will assess the overall response rate in patients with recurrent platinum resistant epithelial ovarian, fallopian tube or primary peritoneal cancer who previously received Avastin. We began enrolling patients into the Phase 2 expansion portion of this trial in July 2016.

A Phase 2 single-arm IST of CRLX101 as monotherapy and in combination with Avastin in patients with relapsed ovarian cancer is being conducted at Massachusetts General Hospital and affiliated Harvard University teaching hospitals. The monotherapy arm of the trial, in which 29 patients were enrolled, met its primary endpoint. The results from the monotherapy arm led to the combination arm of this trial, which employs a two-stage design. The first stage enrolled 18 patients and achieved the pre-defined criterion for advancement into the second stage, which showed improved activity relative to the monotherapy arm. The second stage of this trial is ongoing.

We are also evaluating the combination of CRLX101 with Poly ADP ribose polymerase inhibitors, or PARP inhibitors. PARP inhibitors, such as LYNPARZA™ (olaparib), hinder a cell's ability to repair single-strand DNA breaks. Topo 1 inhibitors, such as CRLX101, create persistent single-strand DNA breaks, and preclinical experiments have shown that PARP inhibition potentiates the DNA damage resulting from topo 1 inhibition. PARP-topo 1 combinations have traditionally been limited by toxicity. However, we believe our NDC platform may enable a therapeutic PARP-topo 1 combination because NDC's are designed to concentrate anti-cancer payloads inside tumor cells and spare healthy tissue. Preclinical data generated by AstraZeneca AB, or AstraZeneca, with a LYNPARZA-CRLX101 combination demonstrated a synergistic anti-tumor effect from targeting two validated pathways. Based on this data, in November 2015, we entered into a collaboration agreement with the National Cancer Institute, or the NCI, and AstraZeneca to study the LYNPARZA-CRLX101 combination in human clinical trials.

In May 2016, we announced that the first patient was dosed in an open-label, single center Phase 1/2 clinical trial of CRLX101 in combination with LYNPARZA in patients with advanced solid tumors. This trial is being conducted by the NCI. We believe that with our NDC and the work AstraZeneca has done to define a clinical dose and schedule, we may be able to develop an effective and tolerable LYNPARZA-CRLX101 combination. The Phase 1 portion of this clinical trial will enroll up to 30 patients with advanced solid tumors that are resistant or refractory to standard therapy. The trial is designed to identify the MTD, or recommended Phase 2 dose, of CRLX101 when combined with LYNPARZA, and to provide additional data on pharmacokinetics, pharmacodynamics and safety. The Phase 2a portion will evaluate the efficacy of this combination in relapsed small cell lung cancer patients dosed at the identified recommended Phase 2 dose and schedule.

Our second platform-generated NDC clinical candidate, CRLX301, is an NDC with docetaxel as its anti-cancer payload. CRLX301 is designed to concentrate in tumors and slowly release docetaxel inside tumor cells. We are studying CRLX301 in a Phase 1/2a trial in patients with advanced solid tumor malignancies in order to evaluate the safety of the drug and establish an MTD for two dosing schedules. In the Phase 1 stage of the clinical trial we explored tolerability of dose ranges when the drug candidate was administered once every three weeks and have determined an MTD for this dosing schedule. We are also exploring a weekly dosing schedule as part of the Phase 1 stage to determine the MTD for that regimen. These parallel paths will allow us to determine the recommended Phase 2 dose with the preferred dosing schedule.

In June 2016, we announced that we had dosed the first patient in the Phase 2a stage of this clinical trial, evaluating a once every three weeks dosing schedule. The Phase 2a expansion includes two stages. In Stage 1 we plan to enroll up to eight patients in each dosing schedule. This stage of the trial is designed to further establish the safety and tolerability of each dosing schedule and to provide additional data on pharmacokinetics, pharmacodynamics and antitumor activity. In Stage 2 we plan to enroll up to 36 additional patients with specific tumor types using the optimal dosing schedule.

To date, we have devoted substantially all of our resources to our drug discovery and development efforts, including conducting clinical trials of our product candidates, protecting our intellectual property and the general and administrative support of our operations. We have generated no revenue from product sales. We expect that it will be several years before we commercialize a product candidate, if ever. Through June 30, 2016, we have funded our operations primarily through $84.2 million in proceeds from the sale of shares of our convertible preferred stock in private placements, net proceeds of $59.9 million from sales of shares of our common stock in our initial public offering, or IPO, net proceeds of $37.2 million from the sale of shares of our common stock in April 2015 in an underwritten public offering, or Secondary Offering, $17.3 million in proceeds from our sale of convertible promissory notes, $10.0 million in proceeds from a loan and security agreement with Lighthouse Capital Partners VI, L.P., or Lighthouse Capital, and $21.0 million in proceeds from a loan and security agreement with Hercules Technology Growth Capital, Inc., or Hercules. We refer to our loan and security agreements with Lighthouse Capital and Hercules as the Lighthouse Loan Agreement and the Hercules Loan Agreement, respectively.

We have never been profitable and have incurred significant operating losses since our incorporation. As of June 30, 2016, we had an accumulated deficit of $185.8 million. We incurred net losses of approximately $24.4 million and $18.3 million for the six months ended June 30, 2016 and 2015, respectively.

We expect to continue to incur significant and increasing expenses and operating losses for the foreseeable future, as we advance our product candidates through preclinical studies and clinical trials, and as we seek regulatory approval for, and eventually commercialize, our product candidates. Our net losses may fluctuate significantly from quarter to quarter and from year to year. We will need to raise additional capital in the future to support our expenses and operating activities.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the next several years, if ever. In the future, we may generate revenue from a combination of product sales, license fees, milestone and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of any such payments. Our ability to generate product revenues will depend on the successful development and eventual commercialization of our product candidates. If we fail to complete the development of our product candidates in a timely manner or to obtain regulatory approval for our product candidates, our ability to generate future revenue and our results of operations and financial position would be materially adversely affected.

To date, our only revenue has consisted of a government tax credit that we received in 2010 and payments in each of the years from 2011 through 2014 from material transfer agreements and/or a research agreement.

Research and Development Expenses

Research and development expense consists of costs incurred in connection with the discovery and development of our Dynamic Tumor Targeting Platform and our NDCs. These expenses consist primarily of:

- employee-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, or CROs, investigative sites that conduct our clinical trials and consultants that conduct a portion of our preclinical studies;
- expenses relating to scientific and medical consultants and advisors;
- the cost of acquiring and manufacturing clinical trial materials;
- facilities, depreciation of fixed assets and other allocated expenses, including direct and allocated expenses for rent and maintenance of facilities and equipment;
- lab supplies, reagents, active pharmaceutical ingredients and other direct and indirect costs in support of our preclinical and clinical activities;
- license fees related to in-licensed products and technology; and
- costs associated with non-clinical activities and regulatory approvals.

We expense research and development costs as incurred.

Conducting a significant amount of research and development is central to our business model. Product candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development primarily due to the increased size and duration of late-stage clinical trials. We plan to increase our research and development expenses for the foreseeable future as we continue to support multiple clinical trials of CRLX101 and CRLX301, and advance our earlier-stage research and development projects.

We use our employee and infrastructure resources across multiple research and development programs. We track external research and development expenses and personnel expense on a program-by-program basis and have allocated expenses such as stock-based compensation and indirect laboratory supplies and services to each program based on the personnel resources allocated to each program. Facilities, depreciation and scientific advisory board fees and expenses are not allocated to a program and are considered overhead. Below is a summary of our research and development expenses 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
CRLX101	$ 5,378	$ 5,030	$ 12,133	$ 8,372
CRLX301	1,116	827	3,217	1,715
Dynamic Tumor Targeting Platform	745	487	1,365	935
Overhead	283	334	577	677
Total research and development expense	$ 7,522	$ 6,678	$ 17,292	$ 11,699

The following summarizes our research and development programs.

CRLX101

Our lead product candidate, CRLX101, is an NDC in Phase 2 clinical development in our two lead indications, relapsed RCC and relapsed ovarian cancer. We are also pursuing development of CRLX101 in combination with anti-cancer therapies in other earlier stage clinical trials that include company-sponsored trials and ISTs.

Our leading CRLX101 development programs are:

- Relapsed RCC:
  - We are conducting a Phase 2 randomized, controlled, company-sponsored trial comparing CRLX101 administered in combination with Avastin to investigator's choice of standard of care in patients with RCC who have received two or three prior lines of therapy.
- Relapsed ovarian cancer:
  - We are conducting a Phase 1b/2 company-sponsored trial of CRLX101 in combination with weekly paclitaxel in patients with relapsed ovarian cancer in collaboration with the GOG.
  - We are also conducting a Phase 2 single-arm IST of CRLX101 as monotherapy and in combination with Avastin in patients with relapsed ovarian cancer at Massachusetts General Hospital and affiliated Harvard University teaching hospitals.

Additional trials involving CRLX101 are also ongoing, including a Phase 1b company-sponsored trial exploring a dose-intensive schedule for CRLX101 in patients with solid tumors, a Phase 1/2 clinical trial sponsored by the NCI, evaluating the combination of CRLX101 and LYNPARZA™ (olaparib) in patients with advanced solid tumors, and a Phase 1b/2 IST in patients with locally advanced rectal cancer.

We cannot accurately project future research and development expenses for our CRLX101 program because such expenses are dependent on a number of variables, including, among others, the cost and design of any additional clinical trials, the duration of the regulatory process and the results of any clinical trials.

Under our license agreement with Calando Pharmaceuticals, Inc., or Calando, pursuant to which we obtained rights to CRLX101, or the CRLX101 Agreement, we are obligated to pay milestone payments which could total, in the aggregate, $32.8 million, if we achieve certain development and sales events with CRLX101. In addition, under the CRLX101 Agreement, if we, or one of our affiliates, sell CRLX101, we are required to pay tiered royalty payments ranging from low- to mid-single digits, as a percentage of worldwide net sales, depending on whether there is patent protection for CRLX101 at the time of the sale. In the event we license or sublicense the intellectual property that we purchased or licensed from Calando, we are required to pay Calando a percentage of the income we receive from the licensee or sublicensee to the extent attributable to such license or sublicense, subject to certain exceptions. The percentage of such license income that we are obligated to pay Calando ranges from the low- to mid-double digits depending on the development stage of CRLX101 at the time we first provide or receive draft terms of a license arrangement with the third party that results in a license agreement.

CRLX301

We are studying CRLX301 in a Phase 1/2a trial in patients with advanced solid tumor malignancies in order to evaluate the safety of the drug and establish an MTD for two dosing schedules. In the Phase 1 stage of the clinical trial we explored tolerability of dose ranges when the drug candidate was administered once every three weeks and have determined an MTD for this dosing schedule. We are also exploring a weekly dosing schedule as part of the Phase 1 stage of the trial to determine the MTD for that regimen. These parallel paths will allow us to determine the recommended Phase 2 dose with the preferred dosing schedule. The Phase 2a expansion of this clinical trial includes two stages. Stage 1 is designed to further establish the safety and tolerability of each dosing schedule and to provide additional data on pharmacokinetics, pharmacodynamics and antitumor activity. Stage 2 will enroll additional patients with specific tumor types using the optimal dosing schedule.

Under our license agreement with Calando pursuant to which we obtained rights to Calando's cyclodextrin system for purposes of conjugating or complexing certain other therapeutic agents to the system, or the Platform Agreement, we paid a $250,000 clinical development milestone to Calando in January 2015 in connection with the initiation of our Phase 1/2a clinical trial of CRLX301 in December 2014. We are also required to make milestone payments in an aggregate amount of up to approximately $18.0 million to Calando if we achieve certain development and sales events with respect to CRLX301. Further, under the Platform Agreement, if we, or one of our affiliates, sell CRLX301 we are required to pay tiered royalty payments ranging from low- to mid-single digits, as a

percentage of worldwide net sales, depending on whether there is patent protection at the time of the sale. In the event we license or sublicense the intellectual property that we purchased or licensed from Calando, we are required to pay Calando a percentage of the income we receive from the licensee or sublicensee to the extent attributable to such license or sublicense, subject to certain exceptions. The percentage of such license income that we are obligated to pay Calando is in the low-double digits.

Dynamic Tumor Targeting Platform

We expect that the expenses related to our NDCs and the development of our platform will continue to increase as we seek to identify additional targets for preclinical research and add personnel to these projects. We cannot accurately predict future research and development expenses for our NDCs because such costs are dependent on a number of variables, including the success of preclinical studies on any such NDC.

The successful development of any of our NDCs is highly uncertain. As such, at this time, we cannot reasonably predict with certainty the duration and costs of the current or future preclinical studies or clinical trials of any of our NDCs or if, when or to what extent we will generate revenues from any commercialization and sale of any of our NDCs that obtain marketing approval. We may never succeed in achieving regulatory approval for any of our NDCs. The duration, costs and timing of development of our NDCs will depend on a variety of factors, including:

- the scope and rate of progress of our ongoing clinical trials;
- a continued acceptable safety profile of any product candidate once approved;
- the scope, progress, timing, results and costs of researching and developing our NDCs and conducting preclinical and clinical trials;
- results from ongoing as well as any future clinical trials;
- significant and changing government regulation in the United States and abroad;
- the costs, timing and outcome of regulatory review or approval of our NDCs in the United States and abroad;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- our ability to raise additional capital, as and when needed;
- establishment of arrangements with third party suppliers of raw materials and third party manufacturers of finished drug product;
- our ability to manufacture, market, commercialize and achieve market acceptance for any of our NDCs that we are developing or may develop in the future;
- the emergence of competing technologies and products and other adverse market developments; and
- the cost of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims.

Any change in the outcome of any of these variables with respect to the development of an NDC could mean a significant change in the cost and timing associated with the development of that NDC. For example, if the FDA, or a comparable non-U.S. regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the marketing authorization of an NDC, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time to obtain marketing authorization.

As a result of the uncertainties discussed above, we are unable to determine when, or to what extent, we will generate revenues from the commercialization and sale of any of our NDCs. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical data with respect to each NDC, our current financial condition, as well as our ongoing assessment of the NDCs' commercial potential. We will need to raise additional capital in the future in order to complete the development and commercialization of CRLX101 and CRLX301 and to fund the development of our other NDCs, if any.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and related costs for personnel in our executive, finance, business development, marketing, legal, information technology and human resources functions. Other general and administrative

expenses include patent filing, patent prosecution, professional fees for legal, insurance, consulting, information technology, auditing and tax services and facility costs not otherwise included in research and development expenses.

We anticipate that our general and administrative expenses will increase in the future for, among others, the following reasons:

- we expect to incur increased general and administrative expenses to support our research and development activities, which we expect to expand as we continue to pursue the development of our NDCs;
- we expect our general and administrative expenses will continue to increase as a result of increased payroll, expanded infrastructure, higher consulting, legal, accounting and investor relations costs, director compensation and director and officer insurance premiums associated with being a public company; and
- we may begin to incur expenses related to sales and marketing of our NDCs in anticipation of commercial launch before we receive regulatory approval of an NDC.

Interest Income

Interest income consists of interest earned on our cash and cash equivalents. The primary objective of our investment policy is capital preservation.

Interest Expense

Interest expense consists primarily of interest, amortization of debt discount and amortization of deferred financing costs associated with the Hercules Loan Agreement. Interest expense in 2015 also included the write off of debt discount and deferred financing costs associated with the repayment of the debt incurred under the Lighthouse Loan Agreement.

Results of Operations

Comparison of Three Months Ended June 30, 2016 and 2015 (Unaudited)

The following table summarizes our consolidated results of operations for the three months ended June 30, 2016 and 2015, together with the changes in those items in dollars and as a percentage (in thousands, except percentages):

	Three Months Ended June 30,		Change	
	2016	2015	Dollar	%
Revenue	$ —	$ —	$ —	—
Operating expenses:				
Research and development	7,522	6,678	844	13%
General and administrative	2,773	2,717	56	2%
Loss from operations	(10,295)	(9,395)	(900)	10%
Total other expense, net	(564)	(512)	(52)	10%
Net loss	$ (10,859)	$ (9,907)	$ (952)	10%

Research and development. Research and development expense for the three months ended June 30, 2016, was $7.5 million compared to $6.7 million for the three months ended June 30, 2015, an increase of $0.8 million, or 13%. The following table summarizes our research and development expense by program for the three months ended June 30, 2016 and 2015, together with the change in spending by program in dollars and as a percentage (in thousands, except percentages):

	Three Months Ended June 30,		Change	
	2016	2015	Dollar	%
CRLX101	$ 5,378	$ 5,030	$ 348	7%
CRLX301	1,116	827	289	35%
Dynamic Tumor Targeting Platform	745	487	258	53%
Overhead	283	334	(51)	-15%
Total research and development expense	$ 7,522	$ 6,678	$ 844	13%

For the three months ended June 30, 2016, CRLX101 program expenses increased by $0.4 million, or 7%, to $5.4 million compared to $5.0 million for the three months ended June 30, 2015. The increase in CRLX101 program expenses was primarily attributable to chemistry, manufacturing, and controls, or CMC, for which costs increased $1.2 million, reflecting increased production and activity to support current and future clinical development of CRLX101. Salary and benefits expenses also increased $0.5 million, reflecting increased headcount, and consulting and other operating costs increased $0.2 million to support the CRLX101 program and the CRLX101 clinical trials. These increases were partially offset by a decrease of $1.6 million in clinical trial expenses, reflecting lower CRO fees, investigator fees and costs associated with clinical sites and laboratories primarily attributable to our RCC Trial.

For the three months ended June 30, 2016, CRLX301 program expenses increased $0.3 million, or 35%, to $1.1 million compared to $0.8 million for the three months ended June 30, 2015. The increase in CRLX301 program expense was primarily attributable to an increase of $0.2 million in CMC costs to support current and future clinical development of CRLX301and an increase of $0.1 million in salary and benefits expenses reflecting increased headcount to support the CRLX301 program and the CRLX301 clinical trials.

Expenses associated with our Dynamic Tumor Targeting Platform were $0.7 million for the three months ended June 30, 2016, an increase of $0.2 million, or 53%, compared to $0.5 million for the three months ended June 30, 2015. The increase was primarily due to increased salary and benefits expenses combined with increases in consulting and external lab costs. Overhead costs decreased $51,000, or 15%, to $0.3 million for the three months ended June 30, 2016 as compared to the three months ended June 30, 2015. The decrease was primarily attributable to a decrease in facility costs.

General and administrative. General and administrative expense for the three months ended June 30, 2016, was $2.8 million compared to $2.7 million for the three months ended June 30, 2015, an increase of $0.1 million, or 2%. The increase in general and administrative costs was primarily attributable to an increase in salary and benefits expenses of $0.2 million, partially offset by a decrease of $0.1 million in facility costs and other general and administrative costs.

Other expense, net. Other expense, net for the three months ended June 30, 2016, was $0.6 million, an increase of $0.1 million, or 10%, compared to $0.5 million for the three months ended June 30, 2015. For the three months ended June 30, 2016 and 2015, other expense, net, was primarily interest expense associated with the Hercules Loan Agreement, including $0.1 million for the amortization of debt discount and deferred financing costs.

Comparison of Six Months Ended June 30, 2016 and 2015 (Unaudited)

The following table summarizes our consolidated results of operations for the six months ended June 30, 2016 and 2015, together with the changes in those items in dollars and as a percentage (in thousands, except percentages):

	Six Months Ended June 30,		Change	
	2016	2015	Dollar	%
Revenue	$ —	$ —	$ —	—
Operating expenses:				
Research and development	17,292	11,699	5,593	48%
General and administrative	5,891	5,398	493	9%
Loss from operations	(23,183)	(17,097)	(6,086)	36%
Total other expense, net	(1,218)	(1,238)	20	(2)%
Net loss	$ (24,401)	$ (18,335)	$ (6,066)	33%

Research and development. Research and development expense for the six months ended June 30, 2016, was $17.3 million compared to $11.7 million for the six months ended June 30, 2015, an increase of $5.6 million, or 48%. The increase was primarily attributable to an increase in costs associated with the CRLX101 program. The following table summarizes our research and development expense by program for the six months ended June 30, 2016 and 2015, together with the change in spending by program in dollars and as a percentage (in thousands, except percentages):

	Six Months Ended June 30,		Change	
	2016	2015	Dollar	%
CRLX101	$ 12,133	$ 8,372	$ 3,761	45%
CRLX301	3,217	1,715	1,502	88%
Dynamic Tumor Targeting Platform	1,365	935	430	46%
Overhead	577	677	(100)	(15)%
Total research and development expense	$ 17,292	$ 11,699	$ 5,593	48%

For the six months ended June 30, 2016, CRLX101 program expenses increased by $3.7 million, or 45%, to $12.1 million compared to $8.4 million for the six months ended June 30, 2015. The increase in CRLX101 program expenses was primarily attributable to CMC, for which costs increased $3.2 million, reflecting increased production and activity to support current and future clinical development of CRLX101. Salary and benefits expenses also increased $0.6 million, reflecting increased headcount to support the CRLX101 program and the CRLX101 clinical trials. These increases were partially offset by a decrease of $0.3 million in clinical trial expenses, reflecting a decrease in CRO fees, investigator fees and costs associated with clinical sites and laboratories.

For the six months ended June 30, 2016, CRLX301 program expenses increased $1.5 million, or 88%, to $3.2 million compared to $1.7 million for the six months ended June 30, 2015. The increase in CRLX301 program expense was attributable to an increase of $0.7 million in salary and benefits expenses reflecting increased headcount to support the CRLX301 program and the CRLX301 clinical trials, an increase of $0.4 million in CMC costs to support current and future clinical development of CRLX301 and an increase of $0.2 million in clinical trial expenses, consisting primarily of increases in CRO and laboratory costs.

Expenses associated with our Dynamic Tumor Targeting Platform were $1.4 million for the six months ended June 30, 2016, an increase of $0.5 million, or 46%, compared to $0.9 million for the six months ended June 30, 2015. The increase was primarily due to increased salary and benefits expenses combined with increases in consulting and external lab costs. Overhead costs decreased $0.1 million, or 15%, to $0.6 million for the six months ended June 30, 2016 compared to $0.7 million for the six months ended June 30, 2015. The decrease was primarily attributable to a decrease in facility costs.

General and administrative. General and administrative expense for the six months ended June 30, 2016, was $5.9 million compared to $5.4 million for the six months ended June 30, 2015, an increase of $0.5 million, or 9%. The increase in general and administrative costs was primarily due to the growth in our corporate infrastructure to support a larger public company. Salaries and benefits, including stock-based compensation, increased $0.4 million for the six months ended June 30, 2016, reflecting increases in finance and accounting, legal, information technology and corporate communications. Professional and consulting fees increased $0.2 million and facility and other general and administrative expenses decreased $0.1 million for the six months ended June 30, 2016, compared to the prior year.

Other expense, net. Other expense, net was $1.2 million for each of the six months ended June 30, 2016 and 2015. For the six months ended June 30, 2016 and 2015, other expense, net, was primarily interest expense associated with the Hercules Loan Agreement, including $0.3 million in each period for the amortization of debt discount and deferred financing costs. For the six months ended June 30, 2015, interest expense included $0.2 million for the write off of debt discount and deferred financing costs associated with the repayment of the Lighthouse Loan Agreement.

Liquidity and Capital Resources

From our incorporation through June 30, 2016, we raised an aggregate of $230.6 million to fund our operations, of which $84.2 million was from the sale of preferred stock in private placements, $59.9 million was from the IPO, $37.2 million was from the Secondary Offering, $17.3 million was from the sale of convertible promissory notes, $31.0 million was from borrowings under loan and security agreements and $1.0 million was from the private placement of our common stock to Hercules. As of June 30, 2016, we had cash and cash equivalents of approximately $47.2 million.

Indebtedness

On January 8, 2015, we entered into the Hercules Loan Agreement and borrowed $15.0 million from Hercules. We used a portion of those proceeds to repay our outstanding indebtedness under the Lighthouse Loan Agreement.

The Hercules Loan Agreement provided for up to three separate tranches of borrowings, the first of which was funded in the amount of $15.0 million on January 8, 2015. On November 24, 2015, we drew a second tranche in the amount of $6.0 million. We elected not to commence a randomized Phase 2 clinical trial of CRLX101 in combination with chemoradiotherapy on or prior to

December 15, 2015, which was a condition of obtaining an additional tranche in an amount of up to $5.0 million. As a result, we are no longer eligible to borrow this amount under the Hercules Loan Agreement.

Our indebtedness under the Hercules Loan Agreement will mature on July 1, 2018. Each advance under the Hercules Loan Agreement accrues interest at a floating per annum rate equal to the greater of (i) 7.30% or (ii) the sum of 7.30% plus the prime rate minus 5.75%. The Hercules Loan Agreement provided for interest-only payments on a monthly basis until December 31, 2015. Thereafter, payments are payable monthly in equal installments of principal and interest to fully amortize the outstanding principal over the remaining term of the loan, subject to recalculation upon a change in the prime rate. We may prepay the indebtedness under the Hercules Loan Agreement in whole or in part upon seven business days' prior written notice to Hercules. Any such prepayment is subject to a prepayment charge of 2.0% if such prepayment occurs after January 8, 2016, but on or before January 8, 2017, or 1.0% if such prepayment occurs after January 8, 2017. Amounts outstanding during an event of default are payable upon Hercules' demand and shall accrue interest at an additional rate of 5.0% per annum of the past due amount outstanding. At the end of the loan term (whether at maturity, by prepayment in full or otherwise), we shall pay a final end of term charge to Hercules in the amount of 6.7% of the aggregate original principal amount advanced by Hercules.

The Hercules Loan Agreement is secured by substantially all of our assets other than our intellectual property. We have also granted Hercules a negative pledge with respect to our intellectual property, which, among other things, restricts our ability to sell, transfer, assign, mortgage, pledge, lease, grant a security interest in or otherwise encumber our intellectual property, subject to certain exceptions. The Hercules Loan Agreement includes restrictive covenants that may restrict our ability to obtain further debt or equity financing.

Lighthouse Loan Agreement. In 2011, we entered into the Lighthouse Loan Agreement which permitted us to borrow up to an aggregate principal amount of $10.0 million. We borrowed $5.0 million in March 2012 and an additional $5.0 million in August 2012. Interest accrued under the Lighthouse Loan Agreement at an annual rate of 8.25%. We repaid in full our outstanding indebtedness under the Lighthouse Loan Agreement and terminated the agreement on January 8, 2015. There were no prepayment charges associated with the early repayment of the loan.

Plan of Operations and Future Funding Requirements

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, clinical trial costs, contract manufacturing services, third-party clinical research and development services, laboratory and related supplies, legal and other regulatory expenses and general overhead costs, as well as debt service requirements.

We believe our cash and cash equivalents of approximately $47.2 million at June 30, 2016, are sufficient to fund our planned operations into the second quarter of 2017 and that we have the ability to reduce or defer operating expenses as may be needed to fund our operations into the third quarter of 2017. We will need to raise additional capital to continue to fund our long-term operations. Should our operating plan change further, or prove to be inaccurate, then we will be required to reassess our operating capital needs. However, there can be no assurance that we will have the cash resources to fund our operating plan or that additional funding will be available on terms acceptable to us, or at all.

Our future capital requirements will depend on many factors, including:

- the number and development requirements of the NDCs we pursue;
- the scope, progress, timing, results and costs of researching and developing our NDCs, and conducting preclinical studies and clinical trials;
- the costs, timing and outcome of regulatory review of our NDCs;
- the cost and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our NDCs for which we receive marketing approval;
- the revenue, if any, received from commercial sales of any NDCs for which we receive marketing approval;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the scope, costs and timing of the manufacture, supply and distribution of our drug candidates for preclinical studies and clinical trials;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the extent to which we acquire or in-license other medicines and technology;
- our headcount growth and associated costs; and
- the costs of operating as a public company.

Identifying potential NDCs and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our NDCs, if approved, may not achieve commercial success. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and revenue from collaboration arrangements. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or drug candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

The following table sets forth the primary sources and uses of cash for each period set forth below (in thousands):

	Six Months Ended June 30,	
	2016	2015
Net cash used in operating activities	$ (24,501)	$ (15,738)
Net cash used in investing activities	(355)	(337)
Net cash (used in) provided by financing activities	(3,859)	50,377
Net (decrease) increase in cash and cash equivalents	$ (28,715)	$ 34,302

Net Cash Used in Operating Activities

The net use of cash in each period resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was $24.5 million for the six months ended June 30, 2016, compared to $15.7 million for the six months ended June 30, 2015, an increase of $8.8 million, or 56%. The increase in net cash used in operating activities resulted primarily from an increase in operating expenses of $6.1 million, an increase in cash paid for interest of $0.3 million and components of working capital of $3.1 million, partially offset by an increase in stock compensation expense of $0.6 million and an increase in deferred rent of $0.1 million.

Net Cash Used in Investing Activities

Net cash used in investing activities was $0.4 million for the six months ended June 30, 2016, compared to $0.3 million for the six months ended June 30, 2015. For the six months ended June 30, 2016, cash used in investing activities included $0.5 million for purchases of property and equipment, primarily lab equipment, partially offset by a $0.1 million decrease in restricted cash used to collateralize a stand-by letter of credit issued as a security deposit on our former facility lease. Cash used in investing activities for the six months ended June 30, 2015, included $0.1 million for purchases of property and equipment and a $0.2 million increase in restricted cash used to collateralize a stand-by letter of credit issued as a security deposit on our new facility lease.

Net Cash Used in (Provided by) Financing Activities

Net cash used in financing activities was $3.9 million for the six months ended June 30, 2016, compared to net cash provided by financing activities of $50.4 million for the six months ended June 30, 2015. Net cash used in financing activities for the six months ended June 30, 2016 was due to the principal payments of $3.9 million under the Hercules Loan Agreement. Net cash provided by financing activities for the six months ended June 30, 2015, was primarily due to net proceeds of $37.2 million from our Secondary Offering, proceeds of $15.0 million from our initial borrowing under the Hercules Loan Agreement, proceeds of $1.0 million from the sale of our common stock in a private placement to Hercules and proceeds of $1.5 million from the exercise of stock options. Net cash provided by financing activities for the six months ended June 30, 2015, was reduced by $3.9 million paid to repay in full the Lighthouse Loan Agreement and cash paid for debt issuance costs of $0.4 million.

Contractual Obligations and Contingent Liabilities

As of June 30, 2016, there were no material changes, outside of the ordinary course of business, in our outstanding contractual obligations from those disclosed in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Recent Accounting Pronouncements

In March 2016, the Financial Accounting Standards Board, or FASB issued Accounting Standards Update 2016-09, “Improvements to Employee Share-Based Payment Accounting” or, ASU 2016-09. ASU 2016-09 is intended to simplify various aspects of how share-based payments are accounted for and presented in financial statements. The standard is effective prospectively for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2016, with early adoption permitted. We are currently evaluating the effect this standard will have on our consolidated financial statements and related disclosures.

In February 2016, the FASB issued Accounting Standards Update 2016-02, “Leases” or, ASU 2016-02, which provides new accounting guidance on leases. ASU 2016-02 requires lessees to recognize leases on their balance sheets, and leaves lessor accounting largely unchanged. The amendments in ASU 2016-02 are effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early application is permitted for all entities. ASU 2016-02 requires a modified retrospective approach for all leases existing at, or entered into after, the date of initial application, with an option to elect to use certain transition relief. We are currently evaluating the effect this standard will have on our consolidated financial statements and related disclosures.

In August 2014, the FASB issued Accounting Standards Update 2014-15, “Disclosure of Uncertainties About an Entity’s Ability to Continue as a Going Concern”, or ASU 2014-15. ASU 2014-15 requires management to evaluate, at each annual and interim reporting period, whether there are conditions or events that raise substantial doubt about the entity’s ability to continue as a going concern and provide related disclosures. ASU 2014-15 is effective for annual and interim reporting periods beginning January 1, 2017 and is not expected to have a material impact on our consolidated financial statements.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of June 30, 2016, we had cash and cash equivalents, including restricted cash, of approximately $47.4 million, consisting primarily of investments in money market funds and certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of United States interest rates, particularly because our investments are in cash and cash equivalents. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material

effect on the fair market value of our investment portfolio. As of June 30, 2016, we were also subject to interest rate risk from our indebtedness under the Hercules Loan Agreement that accrues interest at a floating per annum rate equal to the greater of (i) 7.30% or (ii) the sum of 7.30% plus the prime rate minus 5.75%. A 10% increase in interest rates at June 30, 2016, would not have a material effect on our annual interest expense.

Item 4. Controls and Procedures.

Disclosure Controls and Procedures

Our management, under the supervision and with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Quarterly Report on Form 10-Q. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosures.

Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our principal executive officer and 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

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended June 30, 2016, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1A. Risk Factors.

Our business is subject to numerous risks. The following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Quarterly Report on Form 10-Q and other filings with the Securities and Exchange Commission, or SEC, press releases, communications with investors and oral statements. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Risks Related to Our Financial Position and Need for Additional Capital

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We will need to raise additional capital to fund any Phase 3 clinical trial of CRLX101 or other clinical trials of CRLX301. We also expect that our expenses will increase in connection with our ongoing activities, particularly as we advance the clinical development of CRLX101 and CRLX301 and continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other future product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. In particular, the costs that may be required for the manufacture of any product candidate that receives marketing approval may be substantial, and manufacturing our nanoparticle-drug conjugates, or NDCs, for commercial sale will require expensive and specialized facilities, processes and materials. Furthermore, relative to previous years when we operated as a private company, we expect to incur significant additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding to advance the development of our product candidates and to fund our continuing operations. We may be unable to raise capital when needed or on attractive terms, and if so we could be forced to delay, reduce or eliminate our ongoing research and development programs, including CRLX101 and CRLX301, or any future commercialization efforts.

We plan to use our current cash and cash equivalents to fund our ongoing research and development efforts. We will be required to expend significant funds in order to advance development of CRLX101, CRLX301 and our other potential product candidates. Our existing cash and cash equivalents will not be sufficient to fund all of the efforts that we plan to undertake, such as additional randomized trials of CRLX101 or CRLX301. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations or licensing arrangements or other sources. Adequate and additional funding may not be available to us on acceptable terms or at all.

On January 8, 2015 we entered into a loan and security agreement, which we refer to as the Hercules Loan Agreement, with Hercules Technology Growth Capital, Inc., or Hercules, and drew the first tranche of $15.0 million under the Hercules Loan Agreement. On November 24, 2015, we drew a second tranche of $6.0 million under the Hercules Loan Agreement. We elected not to commence a randomized Phase 2 clinical trial of CRLX101 in combination with chemoradiotherapy on or prior to December 15, 2015, which was a condition of obtaining an additional tranche in an amount of up to $5.0 million. As a result, we are no longer eligible to borrow this amount under the Hercules Loan Agreement.

If we elect to obtain any additional debt financing, our ability to do so may be limited by covenants we have made under the Hercules Loan Agreement and our pledge to Hercules of substantially all of our assets, other than our intellectual property, as collateral. We have also granted Hercules a negative pledge with respect to our intellectual property, which, among other things, prohibits us from selling, transferring, assigning, mortgaging, pledging, leasing, granting a security interest in or otherwise encumbering our intellectual property. This negative pledge could further limit our ability to obtain additional debt financing. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

On April 10, 2015 we closed an underwritten public offering, or the Secondary Offering, of 6,716,000 shares of common stock, including 876,000 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of $6.00 per share. The gross proceeds to us from the Secondary Offering were approximately $40.3 million, before deducting underwriting discounts and commissions and offering expenses payable by us.

We believe our cash and cash equivalents of approximately $47.2 million at June 30, 2016, are sufficient to fund our planned operations into the second quarter of 2017 and that we have the ability to reduce or defer operating expenses as may be needed to fund our operations into the third quarter of 2017. We will need to raise additional capital to continue to fund our long-term operations. Should our operating plan change further, or prove to be inaccurate, then we will be required to reassess our operating capital needs. However, there can be no assurance that we will have the cash resources to fund our operating plan or that additional funding will be available on terms acceptable to us, or at all.

Our future capital requirements will depend on many factors, including:

- the number and development requirements of the product candidates we pursue;
- the scope, progress, timing, results and costs of researching and developing our product candidates, and conducting preclinical and clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates;
- the cost and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of any product candidates for which we receive marketing approval;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the extent to which we acquire or in-license other medicines and technology;
- our headcount growth and associated costs; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, license and development agreements with collaboration partners or other sources. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect the rights of our existing stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, additional debt financing would result in increased fixed payment obligations.

If we raise funds through collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our existing and any future indebtedness could adversely affect our ability to operate our business.

On January 8, 2015, we entered into the Hercules Loan Agreement and drew the first tranche of $15.0 million. We used $3.6 million of the proceeds from our draw under the Hercules Loan Agreement to repay in full our outstanding indebtedness under our loan and security agreement with Lighthouse Capital Partners VI, L.P. On November 24, 2015 we drew an additional tranche of $6.0

million under the Hercules Loan Agreement. As of June 30, 2016, we had approximately $18.6 million in outstanding indebtedness under the Hercules Loan Agreement.

Our outstanding indebtedness combined with current and future financial obligations and contractual commitments, including any additional indebtedness beyond our borrowings from Hercules, could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, and prepayment and repayment fees and penalties, thereby reducing money available to fund working capital, capital expenditures, product development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents. Nevertheless, we may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under our existing debt instruments. Failure to make payments or comply with other covenants under our existing debt instruments could result in an event of default and acceleration of amounts due. If an event of default occurs and Hercules accelerates the amounts due, we may not be able to make accelerated payments, and Hercules could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all of our assets other than our intellectual property.

We have incurred significant losses since incorporation. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since incorporation, we have incurred significant operating losses. As of June 30, 2016, we had an accumulated deficit of $185.8 million. We do not know whether or when we will become profitable. We have not generated any revenues to date from product sales and have financed our operations primarily through public offerings of our common stock, private placements of our preferred stock, convertible debt financings and secured debt financings. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- initiate and continue company-sponsored clinical trials of CRLX101, our most advanced product candidate, including single-arm trials and randomized controlled trials, alone or in combination with other agents;
- support ongoing and any new investigator-sponsored clinical trials, or ISTs, of CRLX101;
- continue our Phase 1/2a clinical trial of CRLX301, our second most advanced product candidate, as well as subsequent studies of CRLX301;
- meet corresponding manufacturing, shipping and storage requirements;
- elect to expand, amend or redesign any current trial of CRLX101 or CRLX301;
- continue our research and preclinical development of additional product candidates utilizing our Dynamic Tumor Targeting Platform;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- in the future, establish a sales, marketing and distribution infrastructure in the United States;
- scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- add equipment and physical infrastructure to support our research and development; and
- hire additional personnel and/or incur severance costs associated with the termination of employment of any existing personnel.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. We do not expect to generate significant revenue unless and until we are able to obtain marketing approval for, and successfully commercialize, one or more of our product candidates. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates, manufacturing, marketing and selling any products for which we may obtain regulatory approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. We are only in the preliminary stages of most of these activities and have not yet commenced other of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the United States Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could cause our stockholders to lose all or part of their investment.

Given our planned expenditures, including, without limitation, expenditures in connection with our clinical trials of CRLX101 and CRLX301, our independent registered public accounting firm may conclude that there is substantial doubt regarding our ability to continue as a going concern.

We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

Our operations to date have been limited to organizing and staffing our company, developing and securing our technology, raising capital and undertaking preclinical studies and clinical trials of our product candidates. We have not yet demonstrated the ability to successfully complete development of any product candidates, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

Assuming we obtain marketing approval for any of our product candidates, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Our approach to the discovery and development of product candidates based on our Dynamic Tumor Targeting Platform is unproven, and we do not know whether we will be able to develop any products of commercial value.

We are focused on applying our proprietary Dynamic Tumor Targeting Platform to develop drugs that address serious unmet medical needs. We believe that our Dynamic Tumor Targeting Platform has the potential to create drugs that may have significant utility in several cancer indications, particularly in combination with other cancer therapies. While the results of preclinical studies and early-stage clinical trials have suggested that certain of our product candidates may have such utility, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any of our product candidates in later stage clinical trials or in obtaining marketing approval thereafter. For example, we have not yet advanced a compound beyond Phase 2 clinical development. Moreover, the only compound for which we have completed a Phase 2 clinical trial, CRLX101 for the potential treatment of patients with advanced non-small cell lung cancer, or NSCLC, who had progressed through one or two prior regimens of chemotherapy, failed to meet its primary endpoint of improvement in overall survival.

In addition, we have never had a product candidate receive approval or clearance from the FDA or a non-U.S. regulatory authority. While the FDA has approved nanoparticles such as Doxil® (doxorubicin hydrochloride liposome injection) and Abraxane® (nab-paclitaxel), to our knowledge, the FDA has not yet approved a polymeric nanoparticle such as our NDCs, which are a new way of targeting tumors. The regulatory review process for novel product candidates, such as ours, can be more expensive and take longer than for product candidates based on more well-known or extensively studied technologies due to regulatory authorities' lack of

experience with them. As a result, we may be required to conduct additional studies and/or trials beyond those we anticipate and it may take us longer to develop and/or obtain regulatory approval for our existing and any future product candidates than we expect.

We are particularly dependent on the success of our lead product candidate, CRLX101, and our ability to develop, obtain marketing approval for and successfully commercialize CRLX101. If we are unable to develop, obtain marketing approval for or successfully commercialize CRLX101, either alone or through a collaboration, or experience significant delays in doing so, our business could be materially harmed.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of CRLX101 for the treatment of patients with inadequately treated forms of cancer. Our prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize CRLX101. The success of CRLX101 will depend, among other things, on our ability to successfully complete clinical trials of CRLX101. The clinical trial process is uncertain, and failure of one or more clinical trials can occur at any stage of testing. For example, in 2011, we initiated an open-label, randomized Phase 2 clinical trial of CRLX101 as monotherapy in patients with advanced NSCLC who had progressed through one or two prior regimens of chemotherapy. In this Phase 2 clinical trial, CRLX101 failed to meet its primary endpoint of improvement in overall survival of the CRLX101-treated group as compared to the control arm of the study, which was best supportive care.

In addition to the successful completion of clinical trials, the success of CRLX101 will also depend on several other factors, including the following:

- receipt of marketing approvals from the FDA or other applicable regulatory authorities;
- the performance of our future collaborators for CRLX101, if any;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment and management of supply arrangements with third party raw materials suppliers and manufacturers;
- establishment and management of supply arrangements for the delivery of our product candidates both in the United States and internationally;
- establishment and coordination of supply arrangements for the delivery of combination agents and/or standard of care drugs internationally, depending on the jurisdiction;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity both in the United States and internationally;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales if and when approved;
- a continued acceptable safety profile of CRLX101 following any marketing approval;
- commercial acceptance, if and when approved, by patients, the medical community and third party payors;
- establishment of arrangements with third party manufacturers to obtain finished drug products that are appropriately packaged for sale;
- establishing and maintaining pricing sufficient to realize a meaningful return on our investment; and
- competition with other therapies.

If we are unable to develop, receive marketing approval for, or successfully commercialize CRLX101, or experience delays as a result of any of these factors or otherwise, our business could be materially harmed.

If we experience delays or difficulties in the enrollment of patients in clinical trials, we may not achieve our clinical development on our anticipated timeline, or at all, and our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for CRLX101 or any of our other product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- unexpected or serious adverse events that occur in the trials;

- the proximity of patients to sites;
- the eligibility criteria for the trial;
- the design of the trial;
- efforts to facilitate timely enrollment;
- investigators' engagement with, or enthusiasm about, the trial;
- complexity of initiating or expanding trials with sites outside the United States;
- competing trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our ability to achieve our clinical development timeline and goals, including the dates by which we will commence, complete and receive results from clinical trials. Enrollment delays may also delay or jeopardize our ability to commence sales and generate revenues from our product candidates. Any of the foregoing could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

The FDA and other regulatory agencies may require more extensive or expensive trials for our combination product candidates than may be required for single agent pharmaceuticals.

To obtain regulatory approval for a combination product candidate, the FDA typically requires an applicant to show that each active ingredient in an investigational combination drug candidate makes a contribution to the combined investigational drug candidate's claimed effects and that the dosage of each component, including amount, frequency and duration, is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy. This could require us to conduct more extensive and more expensive clinical trials than would be the case for a single agent pharmaceutical. As a result, the need to conduct such trials could make it more difficult and costly to obtain regulatory approval of our combination drug product candidate than of a new drug containing only a single active pharmaceutical ingredient.

We are currently pursuing the clinical development of CRLX101 in combinations with other drugs. For example, we are exploring combinations with Avastin in relapsed renal cell carcinoma and relapsed ovarian cancer, and with paclitaxel in relapsed ovarian cancer. If the FDA revokes its approval of, or if safety, efficacy, manufacturing or supply issues arise with, Avastin, paclitaxel or any other drug that we use in combination with CRLX101, we may be unable to market CRLX101 or may experience significant regulatory delays or supply shortages, and our business could be materially harmed.

If the FDA revokes its approval of Avastin, paclitaxel, or any other approved therapeutic that we use in combination therapy with CRLX101, then we will not be able to market CRLX101 in combination with that agent. If safety or efficacy issues arise with such combination agent, we may experience significant regulatory delays, and the FDA may require us to redesign or terminate the applicable clinical trials. Moreover, if Avastin, paclitaxel, or another potential combination agent for CRLX101, for instance, were to receive regulatory approval in combination with a different therapeutic in any indication for which we are pursuing approval, such approval could impact the feasibility and design of any subsequent clinical trials that we may seek to conduct evaluating CRLX101 in combination with such agent. In addition, if manufacturing, cost or other issues result in a supply shortage of Avastin, paclitaxel or any other combination agent, we may not be able to complete clinical development of CRLX101 on our current timeline or at all.

Even if CRLX101 were to receive regulatory approval and be commercialized for use in combination with an approved combination agent, we would continue to be subject to the risk that the FDA could revoke its approval of such agent, that safety, efficacy, manufacturing, cost or supply issues could arise with one of these therapeutic agents. This could result in CRLX101 being removed from the market or being less successful commercially.

If our hypothesis regarding the role of hypoxia inducible factor, or HIF, in cancer cells proves incorrect, it may adversely affect our ability to commercialize and market CRLX101.

We believe that the anti-cancer activity shown by CRLX101 in preclinical tumor models is due in part to its inhibition of HIF, and we have prioritized the clinical development of CRLX101, among other criteria, on HIF-driven tumor types. In support of this hypothesis in November 2015 we announced at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics that we have shown that CRLX101 inhibits carbonic anhydrase 9 in patient tumors, considered to be a sensor of HIF-1α.

This clinical evidence is consistent with our preclinical data. While HIF-1α has become a target of increasing interest in cancer research and recent research suggests that HIF-1α is a master regulator for many cancer cell survival pathways, the science underlying HIF-1α is based on recent discoveries and not fully understood. Moreover, the exact role of HIF-2α is less well described and understood. If our hypothesis with respect to the role of HIF in cancer cells proves incorrect, CRLX101 may not have the same level of therapeutic benefit as it might otherwise have, and in that case we may be unable to receive marketing approval for, or successfully commercialize, CRLX101, and our business could be materially harmed.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Two of our product candidates are in clinical development, all of our other potential product candidates are in preclinical development, and the risk of failure of all of our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is 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 clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to have a sufficient quantity of our product candidate available when needed, failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of severe or medically or commercially unacceptable adverse events, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable non-U.S. regulatory authority that a drug product is not approvable. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, dose, dosing schedule, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials, we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

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. For example, although a Phase 1/2a clinical trial of CRLX101 supported advancement of CRLX101 as monotherapy into Phase 2 clinical trials for patients with advanced NSCLC who had progressed through one or two prior regimens of chemotherapy, CRLX101 failed to meet its primary endpoint of improvement in overall survival of patients in this indication. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face additional setbacks. For example, although the results of the Phase 1b/2 single-arm IST of CRLX101 in patients with relapsed RCC supported our hypothesis that CRLX101 in combination with Avastin may be effective in this setting, there is no assurance that the RCC Trial will meet its endpoint or further support our registration strategy for CRLX101 in relapsed RCC. Moreover, there are currently multiple open-label ISTs of CRLX101 ongoing, including a Phase 2 open-label IST in patients with relapsed ovarian cancer, consisting of a single-arm trial of CRLX101 as monotherapy and a single-arm combination trial of CRLX101 and Avastin; and a Phase 1b/2 open-label IST of CRLX101 in combination with chemoradiotherapy in patients with locally advanced rectal cancer. Interim investigator-reported data from subsets of the total patient populations in certain of these ISTs have been reported. These ISTs are still in progress and final results are not yet available. The preliminary results reported from the ISTs have in some cases been observed in only a small number of patients and may not be achieved by other patients on these or other clinical trials. There can be no assurance that company-sponsored trials will confirm the data seen in the ISTs.

The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed and protocol amendments, if any, to address such flaws may not be sufficiently timely or corrective. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. For example, we believe that a significant increase in pathologic complete response may be a clinically meaningful endpoint for the treatment of locally advanced rectal cancer, but there can be no assurance that the FDA will agree. Moreover, no drug has yet been approved in this setting.

In addition, for several reasons it may become more challenging to design a timely, successful Phase 3 clinical trial for CRLX101 for patients with relapsed RCC. These factors include differences in the design requirements for a Phase 3 trial as compared to a Phase 2 trial and recent product approvals in this indication, which are significantly impacting the standard of care, as well as the regulatory thresholds for approval in relapsed RCC.

Another challenge is that preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable non-U.S. regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size, type and disease progression of the patient populations, changes in and adherence to the clinical trial protocols, variability in the quality of clinical supply batches and the rate of dropout among clinical trial participants. Any Phase 2, Phase 3 or other clinical trials that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates.

If we experience any of a number of possible unforeseen events in connection with clinical trials of our product candidates, potential marketing approval or commercialization of our product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent marketing approval of our product candidates, including:

- clinical trials of our product candidates may produce unfavorable, incomplete or inconclusive results, such as with our Phase 2 clinical trial of CRLX101 as monotherapy for patients with advanced NSCLC who had progressed through one or two prior regimens of chemotherapy;
- we may decide, or regulators may advise us, to conduct additional clinical trials or we may decide to abandon an indication or development program following changes in the regulatory environment or competitive landscape;
- we may decide to add or to change a dosing schedule for any given clinical trial based on relevant data;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, patient enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our supply of product candidates may be insufficient to complete our clinical trials as planned due to a batch failure, a lack of funds, a change in priorities, planning errors or other reasons;
- our third party contractors, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet our expectations in a timely manner or at all;
- we may decide to make changes to a trial protocol and fail to receive timely approval for the amendment from the applicable institutional review board(s) or ethics committee(s);
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- investigators may deviate from the trial protocol, fail to conduct the trial in accordance with regulatory requirements or misreport study data;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- prospective clinical trial sites may be unwilling to participate in one or more of our combination clinical trials due to a perceived difficulty in obtaining reimbursement from managed care plans, government, or other third party payors;
- patients who enroll in a clinical trial, or the investigators enrolling such patients, may misrepresent the patients' eligibility to participate in the trial or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the enrollment size for the clinical trial or extend the clinical trial's duration;
- for any given trial we may find it necessary to open more clinical trial sites than originally planned;
- we may have to suspend or terminate one or more clinical trials of our product candidates for various reasons, including unfavorable, incomplete or inconclusive data, unexpected delays, a change in priorities, a determination that the path to commercialization is too difficult or uncertain, a lack of sufficient funding, changes in the competitive or regulatory landscape, a finding that the participants are being exposed to unacceptable health risks, unexpected or serious adverse events or other unexpected characteristics of a product candidate;

- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their respective standards of conduct, a finding that the participants are being exposed to unacceptable health risks, unexpected or serious adverse events or other unexpected characteristics of the product candidate or other therapeutic agents used in our clinical trials or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;
- the FDA or comparable non-U.S. regulatory authorities may disagree with our clinical trial design or our interpretation of data from preclinical studies and clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design of our clinical trials;
- the FDA or comparable non-U.S. regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or drugs (whether provided by us or third parties) or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable non-U.S. regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Product development costs for us will increase if we experience delays in testing or pursuing marketing approvals and we may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or 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 and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

We have conducted and intend to conduct additional clinical trials for certain of our product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations or the complexity of regulatory burdens may otherwise adversely impact us.

We have conducted, currently are conducting and intend in the future to conduct, clinical trials outside the United States. Opening trial sites outside the United States may involve additional regulatory, administrative and financial burdens, including compliance with foreign and local requirements relating to regulatory submission and clinical trial practices. For example, in late 2014, we commenced in Australia the Phase 1 portion of a Phase 1/2a clinical trial of CRLX301 in patients with advanced solid tumor malignancies. In addition, in the first half of 2015, we expanded the RCC Trial to South Korea where we opened five additional clinical sites. We expect to continue to conduct clinical trials of our product candidates at sites outside the U.S.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practices, including review and approval by an independent ethics committee and informed consent from trial patients. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical trials conducted outside the United States must be representative of the population for which we intend to seek approval in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. Nonetheless, there can be no assurance that the FDA will accept data from trials conducted outside the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay or permanently halt our development of CRLX101, CRLX301 or any future product candidates.

In addition, the conduct of clinical trials outside the United States could have a significant impact on us. Risks inherent in conducting international clinical trials include:

- foreign regulatory requirements that could burden or limit our ability to conduct our clinical trials;
- increased costs and heightened supply constraints associated with the acquisition of standard of care drugs and/or combination or comparator agents for which we may bear responsibility in certain jurisdictions;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations;

- more burdensome manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- lack of consistency in standard of care from country to country;
- diminished protection of intellectual property in some countries; and
- changes in country or regional regulatory requirements.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA and comparable non-U.S. regulators, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

We are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Comparable non-U.S. regulatory authorities, such as the EMA, impose similar restrictions. We may never receive such approvals. We must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We have not previously submitted a new drug application, or an NDA, to the FDA or similar drug approval filings to comparable non-U.S. regulatory authorities for any of our product candidates.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if (1) we are required to conduct additional or different clinical trials or preclinical testing of our product candidates beyond the trials and testing that we contemplate, (2) we are unable to successfully complete clinical trials or preclinical testing of our product candidates, (3) the results of these trials or tests are unfavorable, incomplete or inconclusive, or (4) there are unacceptable safety concerns associated with our product candidates, we, in addition to incurring additional costs, may:

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

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

In July 2016 we received a second fast track designation for CRLX101 in combination with paclitaxel for the treatment of platinum-resistant ovarian carcinoma, fallopian tube or primary peritoneal cancer. In April 2015 we received our first fast track designation for CRLX101 for the treatment of metastatic RCC following progression through two or three prior lines of therapy. We may seek fast track designation for other indications or other product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, the FDA may still decide not to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from or stated intentions of our clinical development program.

A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of

the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies as a breakthrough therapy, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

If we fail to obtain or maintain orphan drug exclusivity for some of our product candidates, we will miss out on certain valuable incentives including a period of marketing exclusivity as well as federal grants, tax credits and a waiver of Prescription Drug User Fee Act filing fees.

We intend to develop some product candidates that may be eligible for orphan drug designation from the FDA. Under the Orphan Drug Act, the FDA has discretion to designate a product as an orphan drug if it is designed to treat a rare disease or condition, which is defined as a patient population of less than 200,000 in the United States. The applicant that first obtains FDA approval for a designated orphan drug receives marketing exclusivity for use of that drug for the stated condition or disease for a period of seven years and becomes eligible for certain federal grants, tax credits and a waiver of Prescription Drug User Fee Act filing fees.

For our product candidates that are eligible, we plan to rely on the exclusivity period under the Orphan Drug Act to attain a competitive position. If we do not obtain orphan drug exclusivity for our drug products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition and our revenues will be reduced. In May 2015, the FDA granted orphan drug designation to CRLX101 for the treatment of ovarian cancer.

Even though we have obtained orphan drug designation for CRLX101 for the treatment of ovarian cancer, we still may not be the first to obtain marketing approval for any particular orphan indication. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect it from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved and granted orphan drug exclusivity, the FDA can subsequently approve the same drug for the same condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

We may request Priority Review for one or more of our product candidates at the time of the submission of the NDA to the FDA. The FDA may not grant Priority Review for any of our product candidates. Moreover, even if the FDA designated Priority Review for one of our product candidates, that designation may not lead to a faster regulatory review or approval process and, in any event, would not assure FDA approval.

A ten-month standard NDA review clock will begin at the conclusion of the 60 calendar day filing review period that starts on the date the FDA receives the original submission. This means the FDA has a total of twelve months from its receipt of the original submission to take regulatory action. We may be eligible for Priority Review designation for our NDA submission if the FDA determines that our product candidate treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The six-month Priority Review clock will begin at the conclusion of the 60 calendar day filing review period that starts on the date of FDA receipt of the original submission. Therefore, if granted Priority Review, the FDA has a total of eight months to take action on an application rather than the standard total of twelve months. We may request Priority Review for CRLX101 if and when we submit an NDA for CRLX101. Our current clinical development programs in areas of unmet medical need assume CRLX101 and/or CRLX301 will receive Priority Review. The FDA has broad discretion whether or not to grant Priority Review to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Thus, while the FDA has granted Priority Review to other oncology product candidates, CRLX101 or CRLX301 may not receive similar designation. Moreover, even if one of our product candidates is designated for Priority Review, such a designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving Priority Review from the FDA also does not guarantee approval within the eight-month review cycle or thereafter.

We believe we may in some instances be able to secure approval from the FDA or comparable non-U.S. regulatory authorities to use accelerated registration pathways. If unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals.

We anticipate that we may seek an Accelerated Approval development pathway for certain indications for our product candidates. Under the Accelerated Approval provisions in the Federal Food, Drug, and Cosmetic Act, or FDCA, and the FDA's implementing regulations, the FDA may grant Accelerated Approval to a product designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of Accelerated Approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The Accelerated Approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, Accelerated Approval is contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical profile or risks and benefits for Accelerated Approval. If such post-approval studies fail to confirm the drug's clinical profile or risks and benefits, the FDA may withdraw its approval of the drug.

If we choose to pursue Accelerated Approval, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive such Accelerated Approval. There can be no assurance that the FDA will agree that our endpoint is an appropriate surrogate endpoint. There can also be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for Accelerated Approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback that we will continue to pursue or apply for Accelerated Approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for Accelerated Approval, there can be no assurance that such submission or application will be accepted or that any expedited review or approval will be granted on a timely basis, or at all. The FDA or other non-U.S. authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. Even if the FDA agreed that we could pursue an Accelerated Approval registration pathway, we might not be able to fulfill the FDA's requirements with respect to chemistry, manufacturing and controls in a timely manner, which would cause delays, or approval might not be granted because our submission is deemed incomplete by the FDA.

A failure to obtain Accelerated Approval or any other form of expedited development, review or approval for our product candidates would result in a longer time period to commercialize such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Serious adverse events of CRLX101 or any of our product candidates may be identified during clinical development. Further, other unexpected properties of our product candidates may be identified during manufacture or development. Such adverse events or unexpected properties could delay or prevent the continued development and/or marketing approval of any such product candidate.

Serious adverse events caused by, or other unexpected properties of, our product candidates could cause us, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable non-U.S. regulatory authorities. If any of our product candidates is associated with serious adverse events or other unexpected properties, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which those undesirable characteristics would be expected to be less prevalent, less severe or more tolerable from a risk-benefit perspective. If we learn that the manufacture of our product candidates generates unexpected impurities or product degradants, these properties could contribute to serious adverse events and negatively impact our overall development cost and timelines as we address those properties. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause serious or unexpected adverse events and negatively affect overall development costs and timelines, which may even prevent further development of the compound.

Both camptothecin, the anti-cancer payload of CRLX101, and docetaxel, the anti-cancer payload of CRLX301, have been associated with toxicities. These toxicities led to discontinuation of the clinical development in the case of camptothecin and have led to dose adjustments, treatment discontinuation and extensive supportive care in the case of docetaxel. While we believe that our Dynamic Tumor Targeting Platform has the potential to improve the unfavorable adverse event profiles of both camptothecin and docetaxel, if this hypothesis is wrong and we experience unexpected or more severe toxicities in our ongoing clinical trials or in

clinical trials we conduct in the future, whether due to the inclusion of camptothecin or docetaxel or another therapeutic as the anti-cancer payload in our NDCs or otherwise, we may not receive approval to market, or achieve commercial success with respect to, any of our product candidates, which could prevent us from ever generating revenues or achieving profitability. In addition, our Dynamic Tumor Targeting Platform may have other limitations with respect to targeting tumors and limiting exposure of normal tissue to our NDCs' anti-cancer payload. For example, liver tissue has pore sizes that are generally larger than other normal tissue, and therefore, our NDCs and their anti-cancer payloads may preferentially concentrate in the liver.

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

The development of new NDCs based on our Dynamic Tumor Targeting Platform is a key area of research for us. The drug discovery that we are conducting using our Dynamic Tumor Targeting Platform may not be successful in creating compounds that have commercial value or therapeutic utility. Our research programs may initially show promise in creating potential product candidates, yet fail to yield viable product candidates for clinical development for a number of reasons, including:

- newly designed NDCs may not demonstrate satisfactory efficacy or other benefits, either alone or in combination with other therapeutics; or
- potential product candidates may, on further study, be shown to have harmful toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance.

To identify new product candidates, our research programs will require substantial technical, financial and human resources. We may be unsuccessful in our efforts to identify new potential product candidates. In addition, we may focus our efforts and resources on one or more potential product candidates that ultimately prove to be unsuccessful. If we are unable to identify suitable additional compounds for preclinical and clinical development, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price.

Even if one of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third party payors and others in the medical community necessary for commercial success or the market opportunity for the product candidate may be smaller than we estimate.

We have never commercialized a product. Even if CRLX101 or any of our other product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and may not become profitable. The degree of market acceptance of CRLX101 or any of our other product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- our ability to offer the product for sale at competitive prices;
- our ability to establish and maintain pricing sufficient to realize a meaningful return on our investment;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- the strength of sales, marketing and distribution support;
- the availability of alternative treatments already approved or approval of other new products for the same indications;

- changes in the standard of care for the targeted indications for the product;
- the timing of market introduction of our approved products as well as competitive products and other therapies;
- availability and amount of reimbursement from government payors, managed care plans and other third party payors;
- the strength and efficacy of our marketing and distribution efforts;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

The potential market opportunities for our product candidates are difficult to estimate precisely. Our estimates of the potential market opportunities are predicated on many assumptions, including industry knowledge and publications, third party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential market opportunities.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

Clinical trials of our product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or, alternatively, fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the drug is less effective than previously believed or causes undesirable, serious or fatal side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we may be required to recall the drug or change the way the drug is administered;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the drug may become less competitive; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

If we are unable to establish sales, marketing and distribution capabilities or enter into acceptable sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates that we develop, if and when those product candidates are approved.

We do not have a sales, marketing or distribution infrastructure and have limited experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. If approved, we expect to commercialize our lead product candidates in the United States directly with a small and highly focused commercialization organization. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. We expect that we will commence the development of these capabilities prior to receiving approval of any of our product candidates. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. Such a delay may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities,

our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

We expect to seek one or more strategic partners for commercialization of our product candidates outside the United States. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales and marketing capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that receive marketing approval.

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

The development and commercialization of new drug products is highly competitive. We expect that we will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to CRLX101, CRLX301 and any future product candidates that we may seek to develop or commercialize. Specifically, due to the large unmet medical need, global demographics and relatively attractive reimbursement dynamics, the oncology market is fiercely competitive and there are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of cancer. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, have fewer or more tolerable adverse events or are less costly than any product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

Companies with marketed nanotechnology-based oncology products include Celgene Corporation (Abraxane) indicated for breast cancer, NSCLC and pancreatic cancer), Janssen Products, LP (Doxil indicated for ovarian cancer and, in combination with Velcade® (bortezomib), for multiple myeloma), Merrimack Pharmaceuticals, Inc. (Onivyde™ (irinotecan liposomal injection) indicated for pancreatic and colorectal cancer) and Spectrum Pharmaceuticals, Inc. (Marqibo ® (vincristine sulfate liposome injection) indicated for relapsed Philadelphia chromosome-negative acute lymphoblastic leukemia). Companies with nanotechnology-based oncology product candidates in clinical development include, without limitation, BIND Therapeutics, Inc. (BIND 014 for squamous NSCLC, urothelial carcinoma, cholangiocarcinoma, cervical cancer and squamous cell carcinoma of the head and neck), Celator Pharmaceuticals, Inc., which was recently acquired by Jazz Pharmaceuticals (Vyxeos™ for acute myeloid leukemia), Celsion Corporation (ThermoDox® (lyso-thermosensitive liposomal doxorubicin) for liver cancer and breast cancer), Cytimmune Sciences, Inc. (CYT-6091 for NSCLC), Cristal Delivery B.V. d/b/a Cristal Therapeutics (CriPec® docetaxel for oncology), NantPharma (Cynviloq™, which received fast-track designation from the FDA for breast and lung cancer), Nektar Therapeutics (NKTR102 for solid tumors), Nippon Kayku Seizo Co., Ltd. (NK105 in breast cancer), Starpharma Holdings Ltd. (DEP® docetaxel for oncology), and Supratek Pharma Inc. (SP1049C for solid tumors).

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other marketing approval for their product candidates before we are able to obtain approval for our product candidates, which could result in our competitors establishing a strong market position before we are able to enter the market. The competition for CRLX101 in our targeted indications includes the following:

Renal Cell Carcinoma. In relapsed RCC, the FDA-approved therapies commonly used for treatment represent several mechanistic classes — immune checkpoint inhibitors of PD-1, tyrosine kinase inhibitors, or TKIs, including small molecules and antibody to VEGF ligand, Avastin, and inhibitors of mTOR — and there are no approved cytotoxic drugs that we are aware of. For example, Bristol-Myers Squibb Company's PD-1 antibody Opdivo® (nivolumab) is approved in relapsed RCC following progression on one targeted therapy. Exelixis Inc.'s CABOMETYX® (cabozantinib), a TKI, was also recently approved by the FDA in relapsed RCC following progression on a targeted therapy. In addition, Eisai Co., Ltd.'s Lenvima® (lenvantinib), another TKI, was recently approved in second line RCC in combination with Afinitor® (everolimus). There are also several drugs in development that have the potential to obtain FDA marketing approval and change the standard of care. If this occurs, currently available treatments could be displaced and our commercial opportunity could be reduced. Antibodies against PD-1/PD-L1 and CTL-A4 are in late stage development in first line RCC, both as monotherapies and in combination with other agents including Avastin and small molecule TKIs. Bristol-Myers Squibb is also developing Opdivo in combination with Yervoy™ (ipilimumab) in first line, Merck is developing Keytruda® (pembrolizumab) in combination with Votrient® (pazopanib) in first line and Roche is developing a PD-L1 inhibitor, atezolizumab, in combination with Avastin in first line. Argos Therapeutics, Inc. is developing AGS-003, a dendritic cell therapy, in

first line RCC for patients with unfavorable risk. New small molecule TKIs are also in development. TRACON Pharmaceuticals, Inc.'s TRC105, and Acceleron Pharma, Inc.'s dalantercept (the latter two are in combination with Inlyta® (axitinib)) are in development in second line or later stage relapsed RCC. AVEO Pharmaceuticals, Inc. is developing tivozanib in third line.

Although most of these product candidates are being tested for earlier lines of therapy, they also have the potential to change the standard of care in later lines of therapy in advanced RCC, and to impact the regulatory thresholds for product approvals in this setting. These factors could create questions about the optimal sequence of agents and, among other things, could change the role of Avastin in the treatment of RCC or result in existing first-line therapies being prescribed instead of later lines of therapy. Determining the optimal sequence of agents could be further complicated if their approval and/or availability is different in the United States and Europe. If this occurs, it would potentially reduce the commercial opportunity for CRLX101 in relapsed RCC.

Relapsed Ovarian Cancer. In relapsed ovarian cancer, FDA approvals of Avastin with chemotherapy and Lynparza in BRCA mutated patients have changed the standard of care, which could reduce the commercial opportunity for CRLX101 in this indication. In addition, multiple companies are developing other therapeutic candidates, which are at various stages of development. For example, Abbvie Inc., Clovis Oncology, Inc. Medivation Inc., and TESARO Inc. all have PARP inhibitors in development in BRCA mutated ovarian cancer and breast cancer. Based on the recent NOVA trial, we anticipate that Tesaro's PARP inhibitor, niraparib, will be used in the maintenance setting in platinum-sensitive ovarian cancer. However, it is also possible that oncologists would use the agent in the platinum-resistant setting, which could impact our opportunity in relapsed platinum-resistant ovarian cancer. In addition, immune checkpoint inhibitors and other immune-oncology agents are being developed for the treatment of relapsed ovarian cancer. If these agents are approved in earlier lines of therapy, the addressable market for CRLX101 in later lines of therapy could be adversely impacted. ImmunoGen is also developing IMGN853 in folate receptor positive ovarian cancer, OncoMed Pharmaceuticals is developing demcizumab in non-small cell lung cancer and pancreatic cancer, Genentech, Inc. is developing DMOT4039A in pancreatic cancer and relapsed ovarian cancer, and Incyte Pharmaceuticals Inc. is developing the IDO-1 inhibitor, epacadostat, in relapsed ovarian cancer. Although each of these agents has the potential to be used in combination with CRLX101, thereby expanding the market for CRLX101, they also have the potential to compete with CRLX101.

Many of our existing and potential future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If the FDA or comparable non-U.S. regulatory authorities approve generic versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of data exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations." Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical studies. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. Specifically, in cases in which such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference listed drug. While we believe that CRLX101 would be treated as a new chemical entity by the FDA and, therefore, if approved, should be afforded five years of data exclusivity, the FDA may disagree with that conclusion and may approve generic products after a period that is less than five years. Our other product candidates, including CRLX301, may be treated as new chemical entities as well, but at this point we cannot predict the probability of success in that regard. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

CRLX301 is, and any additional product candidate that we may develop in the future may be, an NDC that includes a generically available therapeutic as its anti-cancer payload. If physicians and/or third party payors do not believe our product offers substantial advantages over other therapies incorporating the same generic anti-cancer payload, we may not be able to successfully commercialize our product.

Although we have intellectual property rights, including composition of matter patents, covering our product candidates, if approved, we expect that our product candidates will compete in the same indications against other nanoparticles and delivery platforms incorporating the same generic therapeutics. In particular, if any of our product candidates is approved and becomes commercially successful, other companies may intensify their efforts to develop a competing product that includes the corresponding generic therapeutic. If physicians, rightly or wrongly, do not believe that a product that we develop offers substantial advantages over another nanoparticle or delivery platform incorporating the same generic therapeutic, physicians might not prescribe our product. In addition, third party payors might refuse to provide reimbursement for a product that we develop when another nanoparticle or delivery platform incorporating the same generic therapeutic offers a cheaper alternative therapy in the same indication, or might otherwise encourage use of another nanoparticle or delivery platform incorporating the same generic therapeutic over our product, even if our product possesses favorable pharmaceutical properties.

Even if we are able to commercialize any product candidate that we develop, the product may become subject to unfavorable pricing regulations, third party payor reimbursement practices or healthcare reform initiatives that could harm our business.

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third party payors. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish and maintain pricing sufficient to realize a meaningful return on our investment.

There is significant uncertainty related to third party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some non-U.S. markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize CRLX101 or any other product candidate will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third party payors, such as private health insurers and health maintenance organizations, decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us to decrease the price we might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable non-U.S. regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for any product candidate that we, or others, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any our product candidates for which we obtain marketing approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our financial condition.

Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining informed consents from our clinical trial participants. We will face an even greater risk if we commercially sell any product that we may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- loss of existing clinical trial participants or difficulty in enrolling future clinical trial participants;
- significant costs to defend resulting litigation or to reach a settlement;
- substantial payments to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We maintain general liability, product liability and umbrella liability insurance. Our existing insurance coverage may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage as our risks of exposure increase, which, for example, would happen if and when we begin selling any product candidate that receives marketing approval. In addition, certain types of insurance coverage are becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct ISTs of some of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our drug candidates may delay or impair our ability to obtain regulatory approval for our product candidates.

We rely on academic and scientific research institutions to conduct and sponsor some of our clinical trials relating to some of our product candidates. We do not control the design or administration of ISTs, and our reliance on third parties to conduct ISTs could, depending on the actions of such third parties, jeopardize the quality or timeliness of the clinical data generated and adversely affect our ability to obtain marketing approval from the FDA or other applicable regulatory authorities.

Such arrangements provide us with certain information rights with respect to ISTs, including access to and the ability to use and reference the data resulting from the IST, including for our own regulatory filings. However, we do not control patient enrollment in, or the quality, timing and reporting of the data from, ISTs, nor do we own the data from the ISTs. Moreover, if we are unable to confirm or replicate the results from the ISTs or if negative results are obtained in the ISTs, we would likely be further delayed or prevented from advancing further clinical development of our drug candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our drug candidates, or if the data proves to be unfavorable, incomplete or inconclusive, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

The FDA or non-U.S. regulatory authorities may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by ISTs, or our interpretation of preclinical, manufacturing or clinical data from ISTs. If so, the FDA or other non-U.S. regulatory authorities may require us to obtain and submit additional preclinical, manufacturing, or clinical data before we may initiate our planned trials and/or may not accept such additional data as adequate to initiate our planned trials. Moreover, there is typically no independent review of the results of ISTs. Therefore, the investigators may interpret the results of ISTs more favorably than an independent review would.

Moreover, ISTs of our product candidates may continue even after we commence company-sponsored trials in the same or different indications. To the extent the results of these ISTs are inconsistent with, or different from, the results of our company-sponsored trials, the FDA or a non-U.S. regulatory authority may question the results of the company-sponsored trial, or subject such results to greater scrutiny than it otherwise would. In these circumstances, the FDA or such other non-U.S. regulatory authorities may require us to obtain and submit additional clinical data, which could delay clinical development or marketing approval of the applicable product candidate.

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We currently rely on third party clinical research organizations, or CROs, site management organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. We also rely on these third parties to collect and monitor adverse event data for our clinical trials. We expect to continue to rely on these third parties to conduct our clinical trials. Our agreements with these third parties generally allow the third party to terminate the agreement at any time. If we are required to enter into alternative arrangements because of any such termination the introduction of our product candidates to market could be delayed.

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, we design our clinical trials and will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. We are also required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We also expect to rely on other third parties to manufacture, store and distribute drug supplies for our clinical trials. 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, producing additional losses and depriving us of potential product revenue.

We have entered into collaborations, and may seek to enter into additional collaborations, with third parties for the development and commercialization of our product candidates. If such collaborations are not successful, or we fail to enter into additional collaborations, we may not be able to capitalize on the market potential of our product candidates.

On November 17, 2015 we announced a collaboration with AstraZeneca AB, or AstraZeneca, and the National Cancer Institute, or the NCI, part of the National Institutes of Health, to conduct a Phase 1/2 clinical trial of the combination of Lynparza and CRLX101 in patients with small cell lung cancer. We may seek additional third-party collaborators for development and commercialization of our product candidates. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and certain governmental agencies. We will have limited control over the amount and timing of resources that any of our current or potential future collaborations dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend significantly on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new dosing schedule, dose level or formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe our intellectual property rights or the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination or divestiture, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. While we have entered into a collaboration with AstraZeneca and the NCI to conduct a Phase 1/2 clinical trial of the combination of Lynparza and CRLX101 in patients with small cell lung cancer, we plan to seek further collaborations with pharmaceutical and biotechnology companies or institutions for the development and potential commercialization of CRLX101 or other product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement with a potential collaborator will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our

expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate manufacturing facilities for the production of clinical quantities of CRLX101 or CRLX301 and have limited personnel with manufacturing experience. We currently rely on and expect to continue to rely on third party contract manufacturers to manufacture supplies of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval.

CRLX101 and CRLX301 must be manufactured through complex, multi-step synthesis processes that are time-consuming and involve special conditions at certain stages. Drug substance manufacture requires high potency containment, and drug product manufacture requires high potency containment under aseptic conditions, also referred to as sterile manufacture. Failures in either drug substance manufacture or drug product manufacture, whether on the part of our existing or future manufacturers or as a result of our failure to make timely and effective improvements in our manufacturing processes, could materially delay clinical development or marketing approval of our product candidates or result in our inability to generate sufficient supplies to meet clinical or commercial demands. For example, in 2015 we experienced a CRLX101 drug substance manufacturing failure due to an out-of-specification event, and the process of obtaining a new batch required several months to complete.

We currently rely on one supplier for each stage of this process and have only limited backup supplier options. If our current contract manufacturers cannot perform as agreed, or become unavailable to us for any reason, we may be required to replace such manufacturers. Our agreements with our third party manufacturers can be terminated by us or such manufacturers on short notice. If any of our existing manufacturers should become unavailable to us for any reason or should be unable to secure additional manufacturing capacity in the event of higher than anticipated product demand, we may incur additional cost or delay in identifying or qualifying replacements. In addition, while we believe that our existing supplier of drug substance or an alternative supplier would be capable of continuing to produce drug substance in commercial quantities, we will need to identify a third-party manufacturer capable of providing commercial quantities of drug product. If we are unable to arrange for such a third-party manufacturing source, or fail to do so on commercially reasonable terms, we may not be able to successfully produce and market CRLX101 or any other product candidate or may be delayed in doing so.

Even if we are able to establish such arrangements with third party manufacturers, reliance on third party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the ability of manufacturers to consistently produce intermediates, drug substance or drug product that meet required quality specifications;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, our ability to secure and/or maintain regulatory approval for our product candidates could be adversely affected. Our failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

CRLX101, CRLX301 and any future product candidates that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

In addition, we typically rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a small number of suppliers for certain capital equipment and raw materials that are used in the manufacture of our drugs. Such suppliers may not sell these raw materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Risks Related to our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of non-U.S. countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, and in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not issue as patents that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our owned or licensed issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. The Leahy-Smith Act includes provisions that affect the way patent applications are prosecuted and affect patent litigation. The United States Patent and Trademark Office, or USPTO, recently developed new regulations and procedures to govern administration of the Leahy-Smith Act. However, many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or licensed patent applications and the enforcement or defense of our owned or licensed issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to third party preissuance submissions of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our owned or licensed patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us, or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate, or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our owned or licensed patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file or participate in infringement claims, which can be expensive and time consuming. Any claims we or our licensors assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensor is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or 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 proceeding could put one or more of our owned or licensed patents at risk of being invalidated or interpreted narrowly.

CRLX101, CRLX301 and certain aspects of our platform technology are protected by patents assigned by or exclusively licensed from other companies or institutions. If these third parties terminate their agreements with us or fail to maintain or enforce the underlying patents, or we otherwise lose our rights to these patents, our competitive position and our market share in the markets for any of our approved products will be harmed.

We are a party to several license agreements and certain aspects of our business depend on patents and/or patent applications owned by others. In particular, we hold exclusive licenses from Calando Pharmaceuticals, Inc., or Calando, and California Institute of Technology, or Caltech, and have been assigned certain patents from Calando for CRLX101, CRLX301 and CDP-based product candidates. We also hold an exclusive license from the State University of New York, or SUNY, related to taxane-containing NDCs, such as CRLX301. We are likely to enter into additional license agreements as part of the development of our business in the future. If we are unable to maintain these patent rights for any reason, our ability to develop and commercialize our product candidates could be materially harmed.

Our licensors may not successfully prosecute certain patent applications under which we are licensed and on which our business depends. Even if patents issue from these applications, our licensors may fail to maintain these patents, may decide not to pursue litigation against third party infringers, may fail to prove infringement, or may fail to defend against counterclaims of patent invalidity or unenforceability.

Risks with respect to parties from whom we have obtained intellectual property rights may also arise out of circumstances beyond our control. For example, in March 2014, Calando entered Chapter 7 bankruptcy and, as a result, the intellectual property rights we have obtained from Calando are subject to potential risks that may arise in connection with bankruptcy. For instance, while our ability to develop and/or commercialize our current product candidates and our ability to utilize our platform are not dependent on the rights that we license from Calando, our license agreements with Calando could be rejected in connection with Calando's bankruptcy, in which case, we could, subject to elections and other rights and defenses that may be available to us, lose certain rights granted to us under such licenses. In March 2015, the bankruptcy court granted Calando's bankruptcy trustee's application to retain a broker to help sell Calando's rights in certain assets including its rights in the license agreements with Cerulean. We reserved our rights with respect to any such sale. The bankruptcy trustee has obtained numerous extensions to the deadline to reject, assume or assume and assign executory contracts including our license agreements. The trustee's next deadline is August 11, 2016.

In addition, in spite of our best efforts, our licensors might conclude that we have materially breached our intellectual property agreements and might therefore terminate the intellectual property agreements, thereby removing our ability to obtain regulatory approval and to market products covered by these intellectual property agreements. If our intellectual property agreements are terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors may have the freedom to seek regulatory approval of, and to market, products similar or identical to ours. Moreover, if our intellectual property agreements are terminated, our former licensors and/or assignors may be able to prevent us from utilizing the technology covered by the licensed or assigned patents and patent applications. For example, under our agreements with Calando, which relate to CRLX101 and our platform, if we fail to meet our payment obligations and do not adequately cure such failure, or if we terminate one or both of these agreements, other than for specified safety concerns, we are required to grant Calando an exclusive (even as to Cerulean), royalty-free license under the patent rights assigned pursuant to such terminated agreement and to assign the related IND to Calando. Moreover, if we fail to meet our diligence obligations under one or both of our agreements with Calando, Calando may convert the license to a non-exclusive license, and we will be required to grant Calando a non-exclusive license under the patent rights assigned to us pursuant to such terminated agreement. This could have a material adverse effect on our competitive business position and our business prospects.

If we fail to comply with our obligations in our intellectual property agreements with third parties, we could lose rights that are important to our business.

We are party to multiple intellectual property agreements that impose, and we may enter into additional intellectual property agreements that may impose, various diligence, milestone payment, royalty and other obligations on us. Under our existing intellectual property agreements, we are obligated to pay royalties on the net sales of product candidates or related technologies to the extent they are covered by the agreement. We also have diligence and development obligations under those agreements. If we fail to comply with our obligations under current or future intellectual property agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product that is covered by the agreement or face other penalties under the agreement. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Some intellectual property which we have licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for United States industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.

Some of the intellectual property rights we have licensed may have been generated through the use of United States government funding and may therefore be subject to certain federal regulations. For example, some of the intellectual property rights licensed to us under the SUNY agreement and which are relevant to taxane containing NDCs such as CRLX301 may have been generated using United States government funds. As a result, the United States government may have certain rights to intellectual property embodied in CRLX301 pursuant to the Bayh-Dole Act of 1980. These United States government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the United States government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The United States government also has the right to take title to these inventions if we fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. In addition, the United States government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the United States government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for United States manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or be threatened with, future adversarial proceedings or

litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in timely obtaining such an agreement with each party who in fact develops intellectual property that we regard as our own. Even if timely obtained, such agreements may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, we may lose valuable intellectual property rights or personnel, in addition to paying monetary damages. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, we face the risk of cybercrime. For instance, someone could hack our information networks and gain illicit access to our proprietary information including our trade secrets. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Even if we are successful in prosecuting such claims, any remedy awarded may be insufficient to fully compensate us for the improper disclosure or misappropriation. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor,

we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. Our product candidates are in the early stages of development and are subject to the risks of failure inherent in drug development. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in conducting and managing the clinical trials, and in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third party CROs to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired. For example, if the regulatory landscape in the United States, Europe or Asia shifts unexpectedly, it may adversely affect the feasibility of study arms, standards of care or statistical assumptions currently reflected in our clinical development plans for CRLX101, potentially delaying the development of CRLX101 in a particular indication and increasing the time required to obtain marketing approval for CRLX101.

Even if we successfully complete the necessary clinical trials for a marketing registration in the U.S., the FDA may convene an advisory committee meeting that could influence their approval decision.

Upon submission of an application for marketing approval in the United States, the FDA may convene an advisory committee (public or closed) to provide the FDA with independent advice from outside experts with specific questions regarding a pending review matter. The opinions or advice expressed by the advisory committee, or any voting decision, are not binding and the FDA retains the ultimate approval power over an application. Regardless of the committee meeting outcome or the FDA's final approval decision, public presentation of our data may shed positive or negative light on our application. A negative advisory committee meeting could signal a lower likelihood of approval, although the FDA may still end up approving our application. Conversely, an oncologic drugs advisory committee, or ODAC, could vote in favor of approval and the FDA may still not approve our application. For an expedited review such as priority review, where the FDA's oncology office has moved focus to how quickly a drug might be approved and has commonly completed their review and approved products well before the PDUFA goal date, preparations for an ODAC could slow down approval. For us as the applicant, preparation time for an ODAC could take six months or more of dedicated effort by the program team, management, and consultants, in addition to supporting the FDA's review queries or any other activities in the same timeframe, reducing resource efficiency. It should not be assumed that an application brought in front of the ODAC means that a negative decision is pending. The FDA determines whether or not to have an ODAC meeting depending on the quality of the

application, the results of the clinical trials, and whether similar issues, such as endpoints or trial designs, have been previously discussed at these meetings. The FDA has generally taken more problematic or complicated applications to an ODAC, which allows for presentation of their findings and a public discussion of issues at hand. On occasion, the FDA will convene an ODAC to have the public clearly understand their viewpoint on the particular application and its supporting evidence, or if there is a first in class or first in indication compound under review. Development of an NDC such as CRLX101 or CRLX301 may qualify for such a review, although if intended to address an unmet medical need and the data are supportive, the chances of an ODAC are lower.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our products in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

On June 23, 2016, a referendum held in the United Kingdom resulted in a majority of U.K. voters electing to leave the European Union. While the impact of this non-binding referendum is still not clear, at this point the vote creates additional uncertainty with respect to obtaining marketing approval for the sale of any product in the U.K.

Even if we obtain marketing approval for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation governing the labeling, packaging, storage and promotion of the product and record keeping and submission of safety and other post-market information.

We must comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive regulatory requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA and other regulatory authorities to monitor and ensure compliance with cGMPs.

Accordingly, assuming we receive marketing approval for one or more of our product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and

corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

Regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA and other agencies, including the Department of Justice, closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market our products for unapproved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- suspension of any ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our relationships with healthcare providers, physicians, and third party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians, and third party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return

for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program, or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drug products to report payments and other transfers of value to physicians and teaching hospitals with data collection beginning in August 2013; and
- analogous state and foreign laws and regulations such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug product manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our financial results. 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.

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

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some non-U.S. jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products, if approved, to be cost-effective compared to other available therapies, they may not cover our product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to realize a meaningful return on our investment. The United States government, state legislatures and non-U.S. governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for our products, if approved.

As a result, the marketability of our products, if approved, could suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. Even if favorable coverage and reimbursement status is attained for one or more of our products that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our product candidates are the following.

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- 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 products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding.

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 in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product

candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of our products, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Our employees and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees or consultants, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, provide accurate information to the FDA or comparable non-U.S. regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Misconduct by employees or consultants could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter 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 be in compliance with such laws, standards 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 and results of operations, including the imposition of significant fines or other sanctions.

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 harm 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 for failure to comply with such laws and regulations.

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, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on our executive team, most of whom have been employed by the company for two years or less. The loss of any member of the executive team could impede the achievement of our goals. Any of our employees may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing finance and sales and marketing personnel will also be critical to our success. The loss of the services of key employees could impede the achievement of our research, development and

commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees, including finance and clinical personnel, may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Should we expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, then as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

Should we experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution, then to manage such future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such potential growth, we may not be able to do so effectively. The potential expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to our Common Stock

The market price of our common stock has been and may in the future be volatile and fluctuate substantially.

Our stock price has been and may in the future be volatile. From April 10, 2014 to June 30, 2016, the closing price of our common stock as reported by the NASDAQ Global Market ranged from a high of $10.87 per share to a low of $1.92 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- actual or anticipated results from, and any delays in, our clinical trials, including the ongoing and any new ISTs of CRLX101, the RCC Trial, from which we expect to report top-line data in the third quarter of 2016, or our Phase 1/2a clinical trial of CRLX301, as well as results of regulatory reviews relating to the approval of our product candidates;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- failure or discontinuation of any of our development programs;
- the level of expenses related to any of our product candidates or clinical development programs;
- commencement or termination of any collaboration or licensing arrangement;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures and capital commitments;
- additions or departures of key scientific or management personnel;
- variations in our financial results or those of companies that are perceived to be similar to us;
- new products, product candidates or new uses for existing products introduced or announced by our competitors, and the timing of these introductions or announcements;
- results of clinical trials of product candidates of our competitors;
- general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies;
- regulatory or legal developments in the United States and other countries;
- changes in the structure of healthcare payment systems;

- conditions or trends in the biotechnology and biopharmaceutical industries;
- actual or anticipated changes in earnings estimates, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock; and
- the other factors described in this "Risk Factors" section.

In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in companies' stock prices, securities class-action litigation has often been instituted against such companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

Our executive officers and directors and their affiliates own a significant percentage of our stock and will be able to exercise significant influence over matters submitted to stockholders for approval.

We believe that as of June 30, 2016, our executive officers and directors and their affiliates beneficially owned 22.0% of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to exert a significant degree of influence over matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would substantially influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership could:

- delay, defer or prevent a change in control;
- entrench our management or board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

An active trading market for our common stock may not be sustained.

Although we have listed our common stock on The NASDAQ Global Market, an active trading market for our shares may not be sustained. In the absence of an active trading market for our common stock, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the times they would like to sell. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

A significant portion of our total outstanding shares may be sold into the public market at any point, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, which we refer to as the Securities Act, or to the extent such shares have already been registered under the Securities Act and are held by non-affiliates of ours.

As of June 30, 2016, there were 4,145,988 shares subject to outstanding options. All of these shares under the Securities Act have been registered on a registration statement on Form S-8. These shares can be freely sold in the public market upon exercise, as permitted by any applicable vesting requirements, except to the extent they are held by our affiliates, in which case such shares will become eligible for sale in the public market as permitted by Rule 144 under the Securities Act. Furthermore, as of June 30, 2016, there were 300,564 shares subject to outstanding warrants to purchase common stock. These shares will become eligible for sale in the public market, to the extent such warrants are exercised, as permitted by Rule 144 under the Securities Act. Moreover, holders of approximately 6.3 million shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

We have broad discretion in the use of our cash reserves and may not use them effectively.

Our management has broad discretion to use our cash reserves and could use our cash reserves in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses and these financial losses could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company through 2019. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some, but not all, of the available exemptions. We cannot predict whether investors will find our common stock less attractive if we 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.

In addition, the JOBS Act also provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We are currently incurring and expect to continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a newly public company, we are incurring and expect to continue to incur additional significant legal, accounting and other expenses that we did not incur as a private company. We expect that these expenses will further increase after we are no longer an "emerging growth company." We expect that we will need to hire additional accounting, finance and other personnel in connection with our continuing efforts to comply with the requirements of being a public company, and our management and other personnel will need to continue to devote a substantial amount of time towards maintaining compliance with these requirements. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission and NASDAQ have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. 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.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal

control over financial reporting. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the growth and development of our business. Furthermore, the terms of the Hercules Loan Agreement prohibit us from paying any dividends without the prior written consent of Hercules, and any future debt agreements may also preclude us from paying dividends. Accordingly, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Provisions in our certificate of incorporation, our by-laws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our certificate of incorporation, our bylaws or Delaware law may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions might frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize our board to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

In addition, we are governed by Section 203 of the Delaware General Corporation Law, which prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. We do not have any control over these analysts. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. In addition, if one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

Use of Proceeds

We completed the initial public offering, or IPO, of our common stock pursuant to a Registration Statement on Form S-1 (File No. 333-194442), which was declared effective by the SEC on April 10, 2014. The net offering proceeds to us, after deducting underwriting discounts and commissions and offering expenses, were approximately $59.9 million.

As of June 30, 2016, we had used all of the net proceeds from our IPO, primarily to fund the clinical development of CRLX101, to fund research and development of CRLX301 and for working capital and other general corporate purposes. There was no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act.

Item 6. Exhibits.

The exhibits listed in the Exhibit Index to this Quarterly Report on Form 10-Q are incorporated herein by reference.

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.

CERULEAN PHARMA INC.

Date: August 4, 2016 By: /s/ Christopher D.T. Guiffre

Christopher D.T. Guiffre
President and Chief Executive Officer
(principal executive officer)

Date: August 4, 2016 By: /s/ Gregg Beloff

Gregg Beloff
Interim Chief Financial Officer
(principal financial officer)

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference			Exhibit Number	Filed Herewith
		Form	File Number	Date of Filing		
10.1	Amendment, dated May 27, 2016, to consulting agreement, dated as of May 27, 2015, between the Registrant and Danforth Advisors LLC					X
10.2	Summary of Non-employee Director Compensation Policy					X
31.1	Certification of principal executive officer pursuant to Rule 13a 14(a)/15d 14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	XBRL Instance Document*					X
101.SCH	XBRL Taxonomy Extension Schema Document*					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document*					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document*					X
101.LAB	XBRL Taxonomy Label Linkbase Document*					X
101.PRE	XBRL Taxonomy Presentation Linkbase Document*					X

* Submitted electronically herewith

Exhibit 10.1

CERULEAN

May 27, 2016

Gregg Beloff
Danforth Advisors, LLC
91 Middle Road
Southborough, MA
01772

Dear Gregg:

This letter is in reference to the Consulting Agreement between Cerulean Pharma Inc. ("Cerulean") and Danforth Advisors, LLC dated May 27, 2015 (the "Agreement"). Capitalized terms used herein and not otherwise defined shall have the meaning given such terms in the Agreement.

As Cerulean desires your continued services, you and Cerulean hereby agree to an extension of the term of the Agreement through May 26, 2017.

If this extension meets with your approval, please countersign a copy of this letter and return one copy to the undersigned.

Very truly yours,

CERULEAN PHARMA INC.

By: /s/ Christopher D. T. Guiffre
Christopher D. T. Guiffre
President & CEO

Agreed to:

DANFORTH ADVISORS, LLC

By: /s/ Gregg Beloff
Gregg Beloff
Managing Director

Exhibit 10.2

SUMMARY OF NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

The board of directors (the "Board") of Cerulean Pharma Inc. (the "Company") has approved a non-employee director compensation policy. Under this non-employee director compensation policy, the Company will pay its non-employee directors retainers in cash, unless a director elects to receive his or her retainer for a given calendar year in the form of awards of unrestricted shares of the Company's common stock, as described below. Each non-employee director will receive a retainer for service on the Board and for service on each committee of which the director is a member. The chairmen of the Board and of each committee will receive higher retainers for such service. The amounts of the retainers are as follows:

		Annual Retainer ($)
Board of Directors		
Chairman		65,000
Member		35,000
Committees of the Board of Directors		
Audit	Chair	20,000
	Member	7,500
Compensation	Chair	15,000
	Member	5,000
Nominating and Corporate Governance	Chair	10,000
	Member	3,500
Clinical Advisory	Chair	20,000
	Member	10,000

These retainers are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment shall be prorated for any portion of such quarter during which the director was not serving. The Company will also reimburse its non-employee directors for reasonable travel and other expenses incurred in connection with attending Board and committee meetings.

Each non-employee director may elect to receive up to 100% of these retainers in the form of awards of unrestricted shares of the Company's common stock, issued on the last day of each quarter for a number of shares of the Company's common stock equal to (x) the amount of the cash retainer that would otherwise have been payable to such director on the date of grant divided by (y) the fair market value of the Company's common stock on the date of grant. Directors wishing to make this election for a given calendar year must make the election on or before the last day of the prior calendar year, except that the election with respect to calendar year 2016 and in any year in which a director is newly elected must be made on or before June 30th of such year or such other date as determined by the Board.

Each director newly elected to the Board will receive an initial option to purchase 22,000 shares of the Company's common stock. Each of these options will vest as to one-third of the shares of our common stock underlying such option on each anniversary of the grant date until the third anniversary of the grant date, subject to the director's continued service as a director, and will become exercisable in full upon a change in control of the Company. Further, on the date of each annual meeting of stockholders, each director that has served on the Board for at least six months will receive an option to purchase 20,000 shares of the Company's common stock. Each of these options will vest in full on the earlier of the first anniversary of the date of grant or immediately prior to the Company's first annual meeting of stockholders occurring after the date of grant, subject to the director's continued service as a director, and will become exercisable in full upon a change in control of the Company.

The exercise prices of the options granted under the Company's non-employee director compensation policy will equal the fair market value of the Company's common stock on the date of grant.

Exhibit 31.1

CERTIFICATION

I, Christopher D.T. Guiffre, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Cerulean Pharma 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)) 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. 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

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

5. The registrant's other certifying officer 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 4, 2016

/s/ Christopher D.T. Guiffre
Christopher D.T. Guiffre
President and Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION

I, Gregg Beloff, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Cerulean Pharma 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)) 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. 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

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

5. The registrant's other certifying officer 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 4, 2016

/s/ Gregg Beloff
Gregg Beloff
Interim Chief Financial Officer
(principal financial officer)

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Cerulean Pharma Inc. (the "Company") for the fiscal quarter ended June 30, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Christopher D.T. Guiffre, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

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

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

Date: August 4, 2016

/s/ Christopher D.T. Guiffre
Christopher D.T. Guiffre
President and Chief Executive Officer
(principal executive officer)

Exhibit 32.2

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

In connection with the Quarterly Report on Form 10-Q of Cerulean Pharma Inc. (the "Company") for the fiscal quarter ended June 30, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Gregg Beloff, Interim Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

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

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

Date: August 4, 2016

/s/ Gregg Beloff
Gregg Beloff
Interim Chief Financial Officer
(principal financial officer)