As filed with the Securities and Exchange Commission on March 31, 2014

Registration No. 333-194442

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

Amendment No. 2
to
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

CERULEAN PHARMA INC.
(Exact name of registrant as specified in its charter)

Delaware	**2834**	**20-4139823**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification No.)**

840 Memorial Drive
Cambridge, MA 02139
(617) 551-9600
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Dr. Oliver S. Fetzer
President and Chief Executive Officer
Cerulean Pharma Inc.
840 Memorial Drive
Cambridge, MA 02139
(617) 551-9600
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Steven D. Singer, Esq.
Lia Der Marderosian, Esq.
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
Telephone: (617) 526-6000

Patrick O'Brien, Esq.
Marko S. Zatylny, Esq.
Ropes & Gray LLP
Prudential Tower
800 Boylston Street
Boston, MA 02199
Telephone: (617) 951-7000

Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 ("Securities Act"), check the following box. ☐

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

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.

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities To Be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)(3)
Common Stock, $0.0001 par value per share	$74,750,000	$9,628

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act.
(2) Calculated pursuant to Rule 457(o) based on a bona fide estimate of the maximum aggregate offering price.
(3) A registration fee of $9,660 was previously paid in connection with this Registration Statement, based on an estimated proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated March 31, 2014

PRELIMINARY PROSPECTUS

CERULEAN

5,000,000 SHARES OF COMMON STOCK

Cerulean Pharma Inc. is offering 5,000,000 shares of its common stock. This is our initial public offering, and no public market currently exists for our shares. We anticipate that the initial public offering price will be between $11.00 and $13.00 per share.

Prior to this offering, there has been no public market for our common stock. We have applied to have our common stock listed on the NASDAQ Global Market under the symbol "CERU."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, and as such are subject to reduced public company disclosure standards. See "Summary—Implications of Being an Emerging Growth Company."

Investing in our common stock involves a high degree of risk. Before buying any shares, you should carefully read the discussion of material risks of investing in our common stock in "Risk Factors" beginning on page 12 of this prospectus.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds to us, before expenses	$	$

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(1) We have agreed to reimburse the underwriters for certain expenses in connection with this offering. See "Underwriting."

Certain of our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to $18.0 million of shares of common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering.

We have granted the underwriters an option for a period of 30 days to purchase up to an additional 750,000 shares of common stock to cover any over-allotments. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to investors on or about , 2014.

Leerink Partners

Canaccord Genuity **JMP Securities** **Wedbush PacGrow Life Sciences**

The date of this prospectus is , 2014.

TABLE OF CONTENTS

You should rely only on the information contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We have not authorized anyone to provide you with different information. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: We have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the "Risk Factors" section beginning on page 12 and our consolidated financial statements and the related notes appearing at the end of this prospectus, before making an investment decision.

As used in this prospectus, unless the context otherwise requires, references to "we", "us", "our", the "company" and "Cerulean" refer to the consolidated operations of Cerulean Pharma Inc., and its consolidated subsidiary, Cerulean Pharma Australia Pty Ltd.

Company Overview

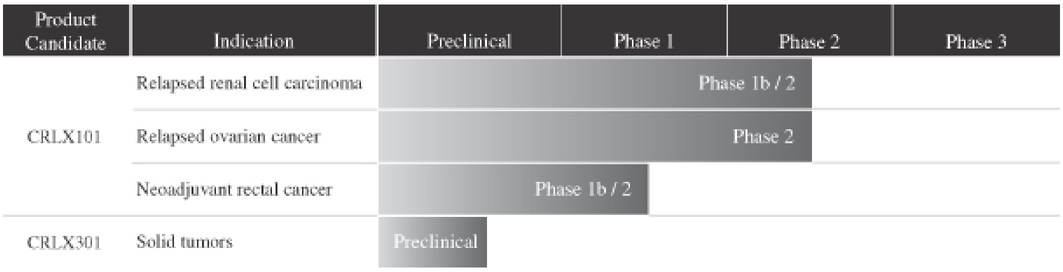
We are a clinical-stage oncology-focused company applying our proprietary dynamic tumor targeting platform to develop differentiated therapies. Our nanopharmaceutical product candidates consist of proprietary polymers that are covalently linked to anti-cancer therapeutics, or payloads. We believe these nanopharmaceuticals dynamically target tumors by exploiting the leakiness of new blood vessels in tumors as an entry portal into tumor tissue, followed by active uptake into tumor cells and the sustained release of the anti-cancer payload inside the tumor cells.

Our lead product candidate, CRLX101, is in Phase 2 clinical development and has the potential to address an unmet need where existing cancer therapies fail. We believe CRLX101, which contains camptothecin as its anti-cancer payload, is a potent, durable and combinable inhibitor of topoisomerase 1, or topo 1, a commercially validated cancer target, and hypoxia inducible factor, or HIF, a novel target of increasing interest in cancer research. Recent research suggests that HIF-1a is a master regulator of multiple cancer cell survival pathways.

CRLX301, the second product candidate from our dynamic tumor targeting platform, is a nanopharmaceutical with docetaxel, a potent and durable microtubule stabilizer, as its anti-cancer payload. We intend to commence a clinical trial of CRLX301 by the end of 2014.

Our Pipeline

The table below summarizes the status of our two lead product candidates. We have global rights to our product candidates.



Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3
CRLX101	Relapsed renal cell carcinoma			Phase 1b / 2	
	Relapsed ovarian cancer			Phase 2	
	Neoadjuvant rectal cancer		Phase 1b / 2		
CRLX301	Solid tumors	Preclinical			

CRLX101

The clinical development of CRLX101 is focused on cancer indications in which the durable inhibition of topo 1 and HIF, in combination with other cancer treatments, is expected to lead to differentiated efficacy. With over 200 patients dosed to date, CRLX101 has demonstrated activity and been well tolerated as monotherapy and in combination with Avastin® (bevacizumab), a leading anti-cancer drug. Initially, we are focusing on combinations with vascular endothelial growth factor, or VEGF, inhibitors or with chemoradiotherapy, where our preclinical studies have demonstrated notable synergies. In addition, we believe CRLX101 may be combinable with other anti-cancer therapies.

We are pursuing development of CRLX101 in combination with anti-cancer therapies in three ongoing clinical development programs:

Relapsed Renal Cell Carcinoma: A Phase 1b/2 open-label investigator sponsored trial, or IST, of CRLX101 in combination with Avastin is being conducted in patients with relapsed renal cell carcinoma. Based on preliminary results from this trial, we believe that the combination of CRLX101 and Avastin may provide therapeutic benefit to relapsed renal cell carcinoma patients. We believe that the therapeutic benefits observed to date in the trial are due to CRLX101's synergy with Avastin and the resulting durable suppression of HIF, topo 1 and VEGF. We intend to commence a randomized, well-controlled Phase 2 clinical trial of CRLX101 in combination with Avastin in the second half of 2014.

Relapsed Ovarian Cancer: A two-part Phase 2 open-label IST of CRLX101 is being conducted in patients with relapsed ovarian cancer. The first part of the trial, a single-arm trial of CRLX101 as monotherapy, has completed enrollment and met its primary progression free survival endpoint with at least four patients having achieved progression free survival time on trial of six months or longer. Platinum-resistant ovarian cancer patients are being enrolled in the second part, a single-arm combination trial of CRLX101 and Avastin. In 2015, assuming positive results from the second part of the trial and adequate additional funding, we expect to initiate a randomized pivotal clinical trial of CRLX101 in combination with Avastin in relapsed platinum-resistant ovarian cancer intended to provide evidence to support regulatory approval in this indication.

Neoadjuvant Rectal Cancer: A Phase 1b/2 open-label IST of CRLX101 in combination with chemoradiotherapy, consisting of Xeloda® (capecitabine) and radiotherapy, is being conducted in patients with rectal cancer who are being treated through the administration of therapeutic agents prior to surgery. We refer to this form of treatment as neoadjuvant therapy, and we refer to patients who receive neoadjuvant therapy as patients with neoadjuvant rectal cancer. In 2015, assuming favorable results from this Phase 1b/2 trial and adequate additional funding, we expect to commence a randomized, well-controlled Phase 2 clinical trial of CRLX101 in combination with chemoradiotherapy.

CRLX301

We intend to advance CRLX301 into a clinical trial by the end of 2014 after we complete the manufacture of clinical supply. Our target product profile for CRLX301 aims to demonstrate improved efficacy, safety and combinability compared to docetaxel, consistent with the results of our preclinical studies, including toxicology in different animal species. We believe that enhanced efficacy and a favorable safety profile for CRLX301 would enable combination therapies with anti-cancer therapies that may not be combinable today due to docetaxel's toxicities. For clinical development of CRLX301, we expect to choose from among those tumor types in which docetaxel is approved and active, in which docetaxel is not approved but where taxanes have demonstrated efficacy or in which resistance to prior taxanes has been established. Such possible tumor types include, among others, breast cancer, prostate cancer, ovarian cancer, melanoma and head and neck cancer.

Other Product Opportunities

In addition to CRLX101 and CRLX301, we have generated additional nanopharmaceuticals using our dynamic tumor targeting platform. These nanopharmaceuticals incorporate small molecules and large molecules, such as RNA, as their payload. We intend to pursue additional product opportunities either by ourselves or in strategic partnerships with pharmaceutical companies to maximize value generation from our platform.

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of nanopharmaceuticals for the treatment of patients with inadequately treated forms of cancer. Key elements of our strategy to achieve this goal are:

- ***Advance the clinical development of our lead product candidate, CRLX101, in multiple tumor types.*** Based on confirmatory signals observed in the ongoing relapsed renal cell carcinoma clinical trial, we plan to initiate a randomized Phase 2 clinical trial of CRLX101 in combination with Avastin in this indication in the second half of 2014. In 2015, we expect to initiate a randomized Phase 2 clinical trial of CRLX101 in combination with chemoradiotherapy in neoadjuvant rectal cancer and a randomized pivotal clinical trial of CRLX101 in combination with Avastin in relapsed platinum-resistant ovarian cancer, assuming continued confirmatory signals from ongoing CRLX101 clinical trials and adequate additional funding.
- ***Advance our second product candidate, CRLX301, into clinical development by the end of 2014.*** We intend to initiate a Phase 1 clinical trial of CRLX301 by the end of 2014. Assuming we are successful in establishing a safe maximum tolerated dose in the Phase 1 trial, we plan to advance CRLX301 into Phase 2 development.
- ***Leverage our platform to discover and develop a proprietary pipeline of highly differentiated product candidates with small molecule anti-cancer payloads.*** Using our dynamic tumor targeting platform, we have created two product candidates, CRLX101 and CRLX301, with small molecule anti-cancer payloads. We have used our platform to create additional nanopharmaceuticals, and we intend over the longer term to develop additional product candidates from the platform.
- ***Leverage our platform beyond our proprietary pipeline to enter into strategic partnerships for the development of product candidates.*** We believe that our platform can be used with a wide range of small and large molecule payloads, such as RNA. While our focus is on oncology, our preclinical data demonstrates that our platform may also be applicable in certain inflammatory diseases. We plan to explore the possibility of entering into partnerships with companies that have proprietary small or large molecule payloads targeting oncology or inflammation indications. We envision selective partnerships with pharmaceutical companies, in which we would leverage the partner’s expertise in combination with our platform, to generate novel nanopharmaceuticals incorporating the partner’s approved therapeutic or development candidate.
- ***Build core capabilities that allow us to commercialize our products in the United States.*** In order to maximize the value of our product candidates, if approved, we expect to commercialize our products in the United States with a focused commercialization organization and to seek one or more strategic partners for commercialization outside the United States.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the “Risk Factors” section of this prospectus immediately following this Prospectus Summary. These risks include the following:

- We have incurred significant losses since our incorporation. We expect to incur losses over the next several years and may never achieve or maintain profitability. As of December 31, 2013, we had an accumulated deficit of $98.4 million.
- 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. In particular, we will need to raise additional funds to conduct our planned Phase 2 clinical trial of CRLX101 in neoadjuvant rectal cancer and pivotal clinical trial of CRLX101 in ovarian cancer. If we elect to obtain any additional debt financing, our ability to do so may be limited by covenants we have made under our loan and security agreement with Lighthouse Capital Partners VI, L.P., or Lighthouse Capital, and our pledge to Lighthouse Capital of substantially all of our assets, other than our intellectual property, as collateral.
- 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 particularly dependent on the success of our product candidate, 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.
- 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. The clinical development of our product candidates is susceptible to the risk of failure inherent in drug development, including failure to demonstrate efficacy, the occurrence of unacceptable adverse events and determination by the FDA or other applicable regulatory authorities that a drug candidate is not approvable.
- We are currently focusing the clinical development of CRLX101 on combinations with Avastin in relapsed renal cell carcinoma and relapsed ovarian cancer and with Xeloda and radiotherapy in neoadjuvant rectal cancer and may focus on additional combinations in the future. If the FDA revokes its approval of, or if safety, efficacy, manufacturing or supply issues arise with, either Avastin or Xeloda, or any other therapeutic that we use in combination with CRLX101 in the future, we may be unable to market CRLX101 or may experience significant regulatory delays or supply shortages, and our business could be materially harmed.
- 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 development 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 rely on third parties to conduct investigator sponsored trials, or ISTs, and other clinical trials 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 do not control the design or administration of ISTs, and our reliance on third parties to conduct the ISTs could, depending on the actions of such third parties, jeopardize the validity of the clinical data generated and adversely affect our ability to obtain marketing approval from the FDA or other applicable regulatory authorities.

- 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.
- CRLX101 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 for any of our approved products will be harmed. In addition, if we fail to comply with our obligations under our intellectual property agreements with third parties, we could lose rights that are important to our business, including our rights to important intellectual property or technology.

Our Corporate Information

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 executive offices are located at 840 Memorial Drive, Cambridge, Massachusetts 02139, and our telephone number is (617) 551-9600. Our website address is www.ceruleanrx.com. The information contained on, or that can be accessed through, our website does not constitute part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Implications of Being an Emerging Growth Company

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we are permitted and intend to rely on exemptions from specified disclosure and other requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- 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 take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1 billion in annual revenue, we have more than $700 million in market value of our stock held by non-affiliates or we issue more than $1 billion of non-convertible debt over a three-year period. We may choose to take advantage of some or all of the available exemptions. We have taken advantage of certain reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision 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 will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

The Offering

Common stock offered	5,000,000 shares
Common stock to be outstanding after this offering	14,305,316 shares
Over-allotment option	The underwriters have an option for a period of 30 days to purchase up to 750,000 additional shares of our common stock to cover over-allotments.
Use of proceeds	We estimate that the net proceeds from this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $53.0 million, or approximately $61.3 million if the underwriters exercise their over-allotment option to purchase additional shares from us in full, assuming an initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus. We plan to use the net proceeds from this offering to fund clinical development of CRLX101, to fund research and development of CRLX301 and other product candidates and for working capital and other general corporate purposes. See "Use of Proceeds" for more information.
Risk factors	You should read the "Risk Factors" section beginning on page 12 of this prospectus and other information in this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Proposed NASDAQ Global Market symbol	"CERU"

The number of shares of our common stock to be outstanding after this offering is based on 786,326 shares of our common stock outstanding as of February 28, 2014 and gives effect to the automatic conversion of all outstanding shares of our preferred stock into 6,826,019 shares of our common stock upon the closing of this offering as well as the issuance of 769,594 shares of common stock issuable upon conversion of our 2013 convertible notes and 923,377 shares of common stock issuable upon conversion of our 2014 convertible notes, each as described below.

The number of shares of our common stock to be outstanding after this offering excludes:

- 128,672 shares of common stock issuable upon exercise of warrants outstanding as of February 28, 2014, at a weighted-average exercise price of $11.50 per share;
- 1,215,315 shares of common stock issuable upon exercise of stock options outstanding as of February 28, 2014, at a weighted-average exercise price of $4.84 per share;
- 6,336 shares of common stock reserved and available as of February 28, 2014 for future issuance under our 2007 stock incentive plan, as amended; and
- 2,400,000 and 500,000 additional shares of our common stock that will be available for future issuance, as of the closing of this offering, under our 2014 stock incentive plan and our 2014 employee stock purchase plan, respectively.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- a one-for-14.5074 reverse stock split of our common stock that was effected on March 31, 2014;
- no exercise of the outstanding options or warrants described above;
- no exercise by the underwriters of their option to purchase up to 750,000 additional shares of our common stock to cover over-allotments;
- the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 6,826,019 shares of our common stock upon the closing of this offering;
- the automatic conversion of our outstanding warrants to purchase 1,857,226 shares of our preferred stock into warrants to purchase an aggregate of 128,672 shares of common stock, upon the closing of this offering;
- the issuance of 769,594 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 7% convertible promissory notes issued in August 2013, or our 2013 convertible notes, upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014;
- the issuance of 923,377 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 7% convertible promissory notes issued in 2014, or our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014; and
- the filing of our restated certificate of incorporation and the adoption of our amended and restated bylaws upon the closing of this offering.

Certain of our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to $18.0 million of shares of common stock in this offering at the initial public offering price. Assuming an initial public offering price of $12.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, these potential purchasers would purchase an aggregate of up to approximately 1,500,000 of the 5,000,000 shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering.

The number of shares of our common stock to be issued upon the automatic conversion of all outstanding principal and accrued interest on our 2013 convertible notes and our 2014 convertible notes upon the closing of this offering depends in part on the initial public offering price of our common stock and the date on which this offering closes. As a result, the actual number of shares of common stock issued upon such conversion may differ from the number of shares set forth above. If the initial public offering price is equal to $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, (1) the outstanding principal and accrued interest on our 2013 convertible notes would convert into an aggregate of 769,594 shares of our common stock upon the closing of this offering and (2) the outstanding principal and accrued interest on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, or $9.30 per share, would convert into an aggregate of 923,377 shares of our common stock upon the closing of this offering, in each case assuming that the offering closes on April 15, 2014. A $1.00 increase in the assumed initial public offering price of $12.00 per share would decrease by 59,200 shares the aggregate number of shares of our common stock issuable upon the automatic conversion of the outstanding principal and interest accrued on our 2013 convertible notes upon the closing of this offering and would decrease by 71,030 shares the aggregate number of shares of our common stock issuable upon the automatic conversion of the outstanding principal and interest accrued on our 2014 convertible notes upon the closing of this offering. A $1.00 decrease in the assumed initial public offering price of $12.00 per share would increase by 69,962 shares the aggregate number of shares of our common stock issuable upon the automatic conversion of the outstanding principal and interest accrued on our 2013 convertible notes upon the closing of this offering and would increase by 83,942 shares the aggregate number of shares of our common stock issuable upon the automatic conversion of the outstanding principal and interest accrued on our 2014 convertible notes upon the closing of this offering.

Summary Consolidated Financial Data

The following summary consolidated financial data for the years ended December 31, 2012 and 2013 and for the period from November 28, 2005 (date of incorporation) to December 31, 2013 (as we are a development stage company) has been derived from our audited consolidated financial statements as of and for the years ended December 31, 2012 and 2013 included elsewhere in this prospectus. The summary consolidated financial data below should be read together with those consolidated financial statements as well as the "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections in this prospectus. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

(in thousands, except share and per share data)	**Years Ended December 31,**		**Period from November 28, 2005 (Date of Incorporation) to December 31, 2013**
	2012	**2013**	
Consolidated Statement of Operations:			
Revenue	$ 625	$ 6	$ 1,669
Operating expenses:			
Research and development	15,807	9,700	67,042
General and administrative	6,393	6,166	31,570
Total operating expenses	22,200	15,866	98,612
Other income (expense):			
Interest income	2	2	684
Interest expense	(567)	(1,487)	(2,395)
Decrease in value of preferred stock warrant liability	39	202	215
Total other (expense) — net	(526)	(1,283)	(1,496)
Net loss	(22,101)	(17,143)	(98,439)
Accretion of redeemable convertible preferred stock	(73)	—	(694)
Net loss attributable to common stockholders	$ (22,174)	$ (17,143)	$ (99,133)
Net loss per share attributable to common stockholders:			
Basic and diluted (1)	$ (36.39)	$ (25.05)	$ (164.80)
Weighted-average common shares outstanding:			
Basic and diluted	609,344	684,330	601,547
Pro forma net loss per share attributable to common stockholders (unaudited):			
Basic and diluted (1)		$ (2.14)	
Pro forma weighted-average common shares outstanding (unaudited):			
Basic and diluted		7,883,204	

(in thousands)	**As of December 31,**			
	2012	**2013**	**Pro Forma (2)**	**Pro Forma As Adjusted (3)(4)**
Consolidated Balance Sheet Data:				
Cash and cash equivalents	$ 16,707	$ 5,488	$ 5,488	$ 67,710
Total assets	$ 17,661	$ 6,827	$ 6,827	$ 68,286
Total liabilities	$ 13,949	$ 19,601	$ 9,615	$ 9,615
Redeemable convertible preferred stock	$ 83,751	$ 81,525	$ —	$ —
Common stock	$ —	$ —	$ 1	$ 1
Additional paid in capital	$ 1,257	$ 4,140	$ 95,650	$ 157,109
Accumulated deficit	$(81,296)	$(98,439)	$ (98,439)	$ (98,439)
Total stockholders (deficit) equity	$(80,039)	$(94,299)	$ (2,788)	$ 58,671

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(1) See notes 2 and 3 within the notes to our consolidated financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net (loss) income per share applicable to common stockholders and pro forma basic and diluted net (loss) income per share applicable to common stockholders.

(2) The pro forma balance sheet data give effect to (i) the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 6,826,019 shares of common stock upon the closing of this offering, (ii) the issuance of 769,594 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 2013 convertible notes upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014, (iii) the issuance of 923,377 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014 and (iv) the conversion of our outstanding warrants to purchase 1,857,226 shares of our preferred stock into warrants to purchase 128,672 shares of common stock upon the closing of this offering.

(3) The pro forma as adjusted balance sheet data give effect to our issuance and sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(4) A $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total assets and total stockholders’ (deficit) equity by approximately $4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should carefully consider the risks and uncertainties described below, together with the other information contained in this prospectus, including our consolidated financial statements and the related notes appearing at the end of this prospectus. If any of the following risks occur, our business, financial condition, results of operations and prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you might lose all or part of your investment.

Risks Related to our Financial Position and Need for Additional Capital

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. Our net loss was approximately $22.1 million for the year ended December 31, 2012 and $17.1 million for the year ended December 31, 2013. As of December 31, 2013, we had an accumulated deficit of $98.4 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 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 the following planned clinical trials of CRLX101, our most advanced product candidate: a Phase 2 clinical trial in combination with Avastin (bevacizumab) in patients with relapsed renal cell carcinoma; a pivotal clinical trial in combination with Avastin in patients with relapsed platinum-resistant ovarian cancer; and a Phase 2 clinical trial in combination with chemoradiotherapy in patients with rectal cancer who are being treated through the administration of therapeutic agents prior to surgery. We refer to this form of treatment as neoadjuvant therapy, and we refer to patients who receive neoadjuvant therapy as patients with neoadjuvant rectal cancer;
- continue to support ongoing investigator-sponsored clinical trials, or ISTs, of CRLX101 in relapsed renal cell carcinoma, relapsed ovarian cancer, neoadjuvant rectal cancer, gastric cancer and small cell lung cancer;
- initiate our planned Phase 1 clinical trial of CRLX301, our second most advanced product candidate;
- continue our research and preclinical development of additional product candidates utilizing our dynamic tumor targeting platform with small and large molecule payloads;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- in the future, establish a sales, marketing and distribution infrastructure and 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;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

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 you to lose all or part of your investment.

In addition, the report of our independent registered public accounting firm with respect to our consolidated financial statements appearing at the end of this prospectus contains an explanatory paragraph stating that our recurring losses from operations, working capital deficiency, accumulated deficit and our need to raise additional financing support prior to June 2014 in order to continue to fund our operations, raise substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient capital in this offering, our business, financial condition and results of operations will be materially and adversely affected and we will need to obtain alternative financing or significantly modify our operational plans to continue as a going concern. Further, even if we successfully complete and receive the net proceeds from this offering, given our planned expenditures for the next several years, including, without limitation, expenditures in connection with our clinical trials of CRLX101, our independent registered public accounting firm may conclude, in connection with the preparation of our financial statements for fiscal year 2014 or any other subsequent period that there is substantial doubt regarding our ability to continue as a going concern.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess 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 you make 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.

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 expect our expenses to increase in connection with our ongoing activities, particularly as we initiate three planned clinical trials of CRLX101, continue to support ISTs of CRLX101, prepare for and initiate a Phase 1 clinical trial of CRLX301 and continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other 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 nanopharmaceuticals for commercial sale will require expensive and specialized facilities, processes and materials. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We plan to use the net proceeds from this offering primarily 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. The net proceeds from this offering and our existing cash and cash equivalents will not be sufficient to fund all of the efforts that we plan to undertake, such as our planned Phase 2 trial of CRLX101 in neoadjuvant rectal cancer and pivotal clinical trial of CRLX101 in ovarian cancer, or to fund completion of clinical development of any of our product candidates. 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. If we elect to obtain any additional debt financing, our ability to do so may be limited by covenants we have made under our loan and security agreement with Lighthouse Capital Partners VI, L.P., or Lighthouse Capital, and our pledge to Lighthouse Capital of substantially all of our assets, other than our intellectual property, as collateral. We have also granted Lighthouse Capital 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.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents as of December 31, 2013, and the proceeds from the convertible notes we issued in 2014, will enable us to fund our operating expenses, debt service and capital expenditure requirements, as set forth below under “Use of Proceeds”, for at least the next 18 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. 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. 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.

Raising additional capital may cause dilution to our stockholders, including purchasers of our common stock in this offering, 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 and/or license and development agreements with collaboration partners. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect your rights as a common stockholder. 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.

As of December 31, 2013, we had $6.7 million of outstanding borrowings under our loan and security agreement with Lighthouse Capital, which we are required to repay in monthly installments through November 2015. We do not intend to use the net proceeds of this offering to prepay any of these borrowings. We could in the future incur additional indebtedness beyond our borrowings from Lighthouse Capital.

Our outstanding indebtedness combined with our other financial obligations and contractual commitments, including any additional indebtedness beyond our borrowings from Lighthouse Capital, 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. 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 Lighthouse Capital accelerates the amounts due, we may not be able to make accelerated payments, and Lighthouse Capital could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all of our assets other than our intellectual property.

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 drugs and with radiotherapy. 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 nanopharmaceuticals, 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 product candidates, if any, than we expect.

We are particularly dependent on the success of our 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 CLRX101 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. This Phase 2 clinical trial 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 of supply arrangements with third party raw materials suppliers and manufacturers;
- establishment of arrangements with third party manufacturers to obtain finished drug products that are appropriately packaged for sale;
- 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;
- 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.

We are currently focusing the clinical development of CRLX101 on combinations with Avastin in relapsed renal cell carcinoma and relapsed ovarian cancer and with Xeloda and radiotherapy in neoadjuvant rectal cancer and may focus on additional combinations in the future. If the FDA revokes its approval of, or if safety, efficacy, manufacturing or supply issues arise with, Avastin, Xeloda, or any other therapeutic that we use in combination with CRLX101 in the future, we may be unable to market CRLX101 or may experience significant regulatory delays or supply shortages, and our business could be materially harmed.

There are ongoing ISTs evaluating CRLX101 (1) in combination with Avastin in patients with relapsed renal cell carcinoma, (2) in combination with Avastin in patients with relapsed ovarian cancer and (3) in combination with Xeloda (capecitabine) and radiotherapy in patients with neoadjuvant rectal cancer, and we expect to commence company-sponsored trials of CRLX101 in combination with Avastin and Xeloda in radiotherapy, as applicable, in these indications. Avastin is currently approved to treat various cancers, and the combination of Xeloda and radiotherapy is currently the standard of care in neoadjuvant rectal cancer in the United States. However, we did not develop or obtain regulatory approval for, and we do not manufacture or sell, Avastin or Xeloda. We may also seek to develop our product candidates in combination with other therapeutics in the future.

If the FDA revokes its approval of either Avastin or Xeloda, we will not be able to market CRLX101 in combination with such revoked therapeutic. If safety or efficacy issues arise with Avastin or Xeloda or any other therapeutics that we seek to combine with our product candidates in the future, we may experience significant regulatory delays, and the FDA may require us to redesign or terminate the applicable clinical trials. If Xeloda and radiotherapy is replaced as the standard of care for treatment of neoadjuvant rectal cancer, the results, if any, of the ongoing IST or our planned company-sponsored clinical trial in neoadjuvant rectal cancer may be less meaningful, and the FDA may require us to conduct additional clinical trials of CLRX101 prior to any regulatory approval in this indication. In addition, if manufacturing or other issues result in a supply shortage of Avastin, Xeloda or any other combination therapeutics, 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 Avastin or Xeloda or another therapeutic, we would continue to be subject to the risk that the FDA could revoke its approval of Avastin or Xeloda, that safety, efficacy, manufacturing or supply issues could arise with one of these therapeutic agents, or that Xeloda and radiotherapy may be replaced as the standard of care in patients with neoadjuvant rectal cancer. This could result in CRLX101 being removed from the market or being less successful commercially.

If our hypothesis regarding the role of 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. While HIF-1a has become a target of increasing interest in cancer research and recent research suggests that HIF-1a is a master regulator for many cancer cell survival pathways, the science underlying HIF-1a is based on recent discoveries and not fully understood. Moreover, the exact role of HIF-2a 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.

One of our product candidates is in clinical development, all of our other 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 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, 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 a Phase 2 clinical trials for patients with advanced non-small cell lung cancer 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. Moreover, there are currently multiple open-label ISTs of CRLX101 ongoing, including: a Phase 1b/2 open-label IST of CRLX101 in combination with Avastin in patients with relapsed renal cell carcinoma; a two-part Phase 2 open-label IST in patients with relapsed ovarian cancer, consisting of a single-arm trial of CLRX101 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 neoadjuvant rectal cancer. Interim investigator-reported data from subsets of the total patient populations in certain of these ISTs have been reported, and such results are described elsewhere in this prospectus. 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. 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 sphincter preservation is a clinically meaningful endpoint for the treatment of neoadjuvant rectal cancer, but there can be no assurance that the FDA will agree. In addition, 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 and type of the patient populations, changes in and adherence to the clinical trial protocols 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.

We intend to conduct, and may in the future conduct, 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.

We have conducted, and may in the future choose to conduct, one or more of our clinical trials outside the United States. For example, we intend to conduct the Phase 1 portion of a Phase 1/2a clinical trial of CRLX301 in patients with advanced solid tumor malignancies at two cancer centers in Australia commencing by late 2014.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this 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 ethical principles. 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 of the United States must be representative of the population for whom 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. Since we currently do not have an active IND in the United States for CRLX301, unless we are able to obtain an active IND, we would be unable to conduct clinical trials in the United States. There can be no assurance that the FDA will accept data from trials conducted outside of the United States and no assurance that we will be successful in obtaining an IND for CRLX301. If the FDA does not accept the data from our Phase1/2a clinical trial of CRLX301 in Australia or any future trial that we determine to conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of 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 restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations; and
- diminished protection of intellectual property in some countries.

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 clinical trials or other testing of our product candidates beyond the trials and testing that we contemplate, (2) we are unable to successfully complete clinical trials of our product candidates or other testing, (3) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, such as in our Phase 2 clinical trial of CRLX101 as monotherapy in patients with non-small cell lung cancer, 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.

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 or inconclusive results, such as with our Phase 2 clinical trial of CRLX101 as monotherapy for patients with advanced non-small cell lung cancer who had progressed through one or two prior regimens of chemotherapy;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- 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 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 their contractual obligations to us in a timely manner or at all;
- 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;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patients who enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial’s duration;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects 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, undesirable side effects or other unexpected characteristics of the product candidate 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;
- 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 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.

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;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical 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.

We may request priority review by the FDA for CRLX101 and may also do so for our other product candidates in the future. The FDA may not grant priority review for CRLX101 or any of our other product candidates. Moreover, even if the FDA designated such products for priority review, that designation may not lead to a faster regulatory review or approval process and, in any event, would not assure FDA approval.

We may be eligible for priority review designation for our product candidates, including CRLX101, if the FDA determines such product candidates offer major advances in treatment or provide a treatment where no adequate therapy exists. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for CRLX101 if and when we submit an NDA for CRLX101. Our current clinical development timeline assumes CRLX101 will receive priority review. The FDA has broad discretion with respect to whether or not to grant priority review status 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 products, CRLX101 may not receive similar designation. Moreover, even if CRLX101 or one of our other 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 does not guarantee approval within the six-month review/approval 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 development 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 pathway for certain of our product candidates. For example, with respect to our development of CRLX101 for the treatment of neoadjuvant rectal cancer, we currently plan to commence a Phase 2 randomized clinical trial by the end of 2014 and to have pathologic complete response data available by late 2015. Assuming positive pathologic complete response data from this Phase 2 trial, we would expect to commence a Phase 3 trial and file an NDA for accelerated approval based on a surrogate endpoint in this Phase 3 trial. Pathologic complete response would be considered a surrogate endpoint under this approach. 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 usually 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 benefit. If such post-approval studies fail to confirm the drug’s clinical benefit, the FDA may withdraw its approval of the drug.

Prior to seeking such accelerated approval, we will 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 pathologic complete response is an appropriate surrogate endpoint or appropriate intermediate clinical endpoint for accelerated approval of CRLX101 for neoadjuvant rectal cancer. 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 or under another expedited regulatory designation (e.g., breakthrough therapy designation), there can be no assurance that such submission or application will be accepted or that any expedited development, 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 conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for CRLX101 for neoadjuvant rectal cancer or any of our other product candidates would result in a longer time period to commercialization of 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 or undesirable side effects or other unexpected properties of CRLX101 or any of our other product candidates may be identified during development that could delay or prevent the product candidate's marketing approval.

Serious adverse events or undesirable side effects 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 undesirable side effects or has properties that are unexpected, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented 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 side effects or other safety or toxicity issues in our ongoing clinical trials or in clinical trials we conduct in the future, whether due to the inclusion of camptotechin or docetaxel or another therapeutic as the anti-cancer payload in our nanopharmaceuticals or otherwise, we may not receive approval to market, or achieve the commercial success we anticipate 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 nanopharmaceuticals' anti-cancer payload. For example, liver tissue has pore sizes that are generally larger than other normal tissue, and therefore, our nanopharmaceuticals may preferentially concentrate in the liver.

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

A significant portion of the research that we are conducting involves the development of new nanopharmaceuticals based on our dynamic tumor targeting platform. 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 nanopharmaceuticals 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 side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance.

Our research programs to identify new product candidates 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 and 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 we 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 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;
- 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 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 other of our product candidates that we may seek to develop or commercialize in the future. 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 side effects 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.

All of the top ten global pharmaceutical companies and most of the mid-size pharmaceutical companies have a strong research and development and commercial presence in oncology. Smaller companies also focus on oncology, including companies such as ARIAD Pharmaceuticals, Inc., Agios Pharmaceuticals, Inc., BIND Therapeutics, Inc., Clovis Oncology, Inc., Endocyte, Inc., Epizyme, Inc., ImmunoGen, Inc., Incyte Corporation, Infinity Pharmaceuticals, Inc., MacroGenics, Inc., Merrimack Pharmaceuticals, Inc., OncoMed Pharmaceuticals, Inc., Onconova Therapeutics, Inc., Pharmacyclics, Inc., Puma Biotechnology, Inc., Seattle Genetics, Inc. and TESARO, Inc.

Several companies are marketing and developing oncology products. Companies with marketed nanopharmaceutical oncology products include Celgene Corporation (Abraxane indicated for breast cancer, NSCLC and pancreatic cancer) and Spectrum Pharmaceuticals (Marqibo® (vincristine sulfate liposome injection) indicated for relapsed Philadelphia chromosome-negative acute lymphoblastic leukemia). Companies with nanopharmaceutical oncology product candidates in clinical development include BIND Therapeutics, Inc. (BIND 014 for NSCLC and metastatic castration-resistant prostate cancer), Celator Pharmaceuticals, Inc. (CPX-351 for acute myeloid leukemia), Celsion Corporation (ThermoDox® (lyso-thermosensitive liposomal doxorubicin) for solid tumors), Cytimmune Sciences, Inc. (CYT-6091 for oncology and autoimmune diseases) and Supratek Pharma Inc. (SP1049C for solid tumors). In addition, at least two companies have clinical-stage oncology product candidates that are irinotecan reformulations: Merrimack Pharmaceuticals' liposomal irinotecan (MM-398 for pancreatic and colorectal cancer) and Nektar Therapeutics' etirinotecan pegol (NKTR102 for breast cancer).

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 products before we are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

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 and certain of our other nanopharmaceutials would be treated as new chemical entities 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. 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, a nanopharmaceutical 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 to 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 time 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 they, 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 overall 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 appropriate 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;
- withdrawal of clinical trial participants;
- significant costs to defend resulting litigation;
- substantial monetary awards 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.

Although we maintain general liability insurance of $2.0 million in the aggregate, umbrella insurance in the amount of $3.0 million in the aggregate and clinical trial liability insurance of $5.0 million in the aggregate, this insurance 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 if and when we begin selling any product candidate that receives marketing approval. In addition, insurance coverage is 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 institutions to conduct and sponsor 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 the ISTs could, depending on the actions of such third parties, jeopardize the validity 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 the ISTs, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we do not control the timing and reporting of the data from ISTs, nor do we own the data from the ISTs. For example, patient enrollment has been slower than we anticipated in the randomized Phase 2 IST comparing CRLX101 as monotherapy to Hycamtin® (topotecan) in advanced small cell lung cancer at the University of Chicago. However, because we are not the sponsor of this trial, we do not control the administration of the trial and have limited or no ability to assist or support patient enrollment. Moreover, if we are unable to confirm or replicate the results from the ISTs or if negative results are obtained, 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 inadequate, 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 will be no independent review of the results of the ISTs. Therefore, the investigators may interpret the results of the 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, to conduct our clinical trials. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, 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, or GCPs, 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 also are 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 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 may seek to enter into collaborations with third parties for the development and commercialization of our product candidates. If we fail to enter into such collaborations, or such collaborations are not successful, we may not be able to capitalize on the market potential of our product candidates.

We may seek 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 and biotechnology companies. We are not currently party to any such arrangement. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would 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 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 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, 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 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. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration 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 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 (i.e., sterile manufacture). In 2013, we experienced a batch contamination issue with the manufacture of a batch of CRLX301 drug substance, and the process of obtaining a new batch has taken several months and is not yet complete. Any additional performance failures on the part of our existing or future manufacturers could delay clinical development or marketing approval of our product candidates. Although we currently have backup suppliers for several stages of the manufacturing process, we rely on one supplier for each stage of this process. 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, 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 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. 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 other products 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 generally 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. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, 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.

Recent 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 PTO, 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 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 other companies or institutions. 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 cyclodextrine polymer-based, or CDP-based, product candidates. We also hold an exclusive license from the State University of New York, or SUNY, related to taxane-containing nanopharmaceuticals, such as CRLX301. In addition, we hold an exclusive license from the Massachusetts Institute of Technology, or MIT, for polymeric nanopharmaceutical-based, or PNP-based, product candidates. 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 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 would have the freedom to seek regulatory approval of, and to market, products similar or identical to ours. Moreover, if our intellectual property agreeements 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 CDP 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 five 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 MIT agreement, and which are relevant to our PNP-based nanopharmaceuticals, may have been generated using United States government funds. In addition, some of the intellectual property rights licensed to us under the SUNY agreement and which are relevant to taxane containing nanopharmaceuticals 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 our current or future PNP-based products or 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.

We currently do not plan to apply for additional United States government funding, but if we do, and we discover compounds or drug candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

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. 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 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.

Failure to obtain marketing approval in international 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.

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. We must therefore 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 FDA 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 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.

The FDA 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 regulates 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 do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDCA 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;
- 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 customers and third party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third party 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 third party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we 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 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 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 government 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;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- 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 false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- federal law requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals;
- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA, requires manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and

- analogous state laws and regulations such as state anti-kickback and false claims laws and analogous non-U.S. fraud and abuse laws and regulations, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and 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 in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

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 manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and non-U.S. 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.

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.

Recently enacted 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.

More recently, in March 2010, President Obama signed into law the PPACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the PPACA of importance to our potential product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the 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;
- extension of manufacturers’ Medicaid rebate liability;
- 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 financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

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 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 employee fraud or other misconduct, 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. Employee misconduct 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 employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to 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 the scientific, business development and clinical expertise of Dr. Oliver Fetzer, our chief executive officer, Mr. Christopher Guiffre, our chief business officer, and Dr. Edward Garmey, our chief medical officer, as well as other principal members of our management, scientific and clinical teams. The loss of this expertise 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 and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other 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 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 and clinical 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.

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

We expect to 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. To manage our anticipated 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 anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The 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 This Offering and Ownership of our Common Stock

We do not know whether a market will develop for our common stock or what the market price of our common stock will be and as a result it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. If a market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors and, as a result of these and other factors, the price of our common stock may fall.

The market price of our common stock may be volatile, which could result in substantial losses for investors purchasing shares in this offering.

The initial public offering price for our common stock will be determined through negotiations with the underwriters. This initial public offering price may vary from the market price of our common stock after the offering. Some of the factors that may cause the market price of our common stock to fluctuate include:

- actual or anticipated results from and any delays in our clinical trials, including the ongoing ISTs of CRLX101, our planned Phase 2 and Phase 3 clinical trials of CRLX101 or our planned Phase 1 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 principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

Following the closing of this offering, our executive officers, directors and principal stockholders, together with their respective affiliates, will beneficially own approximately 59% of our common stock, not including any shares purchased by these stockholders in this offering. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. This concentration of ownership could have the effect of delaying or preventing a change in control of our company or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

Certain of our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to $18.0 million of shares of common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering, and the foregoing discussion does not reflect any potential purchases by these potential purchasers.

A significant portion of our total outstanding shares may be sold into the public market in the near future, 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, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have outstanding 14,305,316 shares of common stock based on the number of shares outstanding as of February 28, 2014. This includes the 5,000,000 shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates or existing stockholders. The remaining 9,305,316 shares are currently restricted as a result of securities laws or lock-up agreements but will become eligible to be sold at various times after the offering. Moreover, after this offering, holders of an aggregate of 7,053,233 shares of our common stock will have rights, subject to specified conditions, to require us to file registration statements covering their shares or, along with holders of an additional 585,091 shares of our common stock, to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the “Underwriting” section of this prospectus.

Certain of our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to $18.0 million of shares of common stock in this offering at the initial public offering price. Any such shares purchased by these potential purchasers may not be able to be resold in the public market immediately following this offering as a result of restrictions under securities laws and lock-up agreements, but would be able to be sold following the expiration of these restrictions as described in the “Shares Eligible for Future Sale” section of this prospectus. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering, and the foregoing discussion does not reflect any potential purchases by these potential purchasers.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of $7.90 per share, representing the difference between the assumed initial public offering price of $12.00 per share and our pro forma net tangible book value per share after giving effect to this offering and the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering as well as the issuance of shares issuable upon conversion of our 2013 convertible notes and 2014 convertible notes and the reclassification of our preferred stock warrant liability, to additional paid in capital, a component of stockholders (deficit) equity. Moreover, we issued warrants and options in the past to acquire common stock at prices significantly below the assumed initial public offering price. As of February 28, 2014, there were 128,672 shares of common stock subject to outstanding warrants with a weighted-average exercise price of $11.50 per share and 1,215,315 shares of common stock subject to outstanding options with a weighted-average exercise price of $4.84 per share. To the extent that these outstanding warrants or options are ultimately exercised, you will incur further dilution.

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 for up to five years. 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:

- providing only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- 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 have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. 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 will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We will 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.

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did not incur as a private company. We expect that we will need to hire additional accounting, finance and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company, and our management and other personnel will need 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. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance. Overall, we estimate that our incremental costs resulting from operating as a public company may be between $2.0 million and $4.0 million per year.

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. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We do not expect to pay any dividends for the foreseeable future. Investors in this offering may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. Furthermore, our loan and security agreement with Lighthouse Capital prohibits us from paying any dividends without the prior written consent of Lighthouse Capital. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We cannot specify with certainty the particular uses of the net proceeds we will receive from this offering. Our management will have broad discretion in the application of the net proceeds, including for any of the purposes described in “Use of Proceeds.” Accordingly, you will have to rely upon the judgment of our management with respect to the use of the proceeds, with only limited information concerning management’s specific intentions. Our management may spend a portion or all of the net proceeds from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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 of 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 you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. These provisions include:

- limitations on the removal of directors;
- a classified board of directors so that not all members of our board are elected at one time;
- advance notice requirements for stockholder proposals and nominations;
- the inability of stockholders to act by written consent or to call special meetings;
- the ability of our board of directors to make, alter or repeal our by-laws; and
- the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could be used to institute a rights plan, or a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors.

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.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.

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 will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “anticipate”, “believe”, “estimate”, “expect”, “intend”, “may”, “plan”, “predict”, “project”, “target”, “potential”, “will”, “would”, “could”, “should”, “continue”, “contemplate”, or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations.

The forward-looking statements in this prospectus include, among other things, statements about:

- our plans to advance the development of, and commercialize, CRLX101, CRLX301 and our other product candidates, including in combination with other drugs and therapies;
- our ongoing and planned preclinical studies and clinical trials;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our plans to leverage our platform to discover and develop additional product candidates;
- our plans with respect to possible future collaborations and partnering arrangements;
- our ability to identify and develop additional product candidates with significant commercial potential;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our expectations relating to the use of proceeds from this offering;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements.

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third party research, surveys and studies generally indicate that the information contained therein has been obtained from sources believed to be reliable, although they do not guarantee the accuracy and completeness of such information. While we believe these industry publications and third party research, surveys and studies are reliable, we have not independently verified such data.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of the common stock that we are offering will be approximately $53.0 million, assuming an initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that our net proceeds will be approximately $61.3 million.

A $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share would increase (decrease) the net proceeds to us from this offering by approximately $4.7 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

As of December 31, 2013, we had cash and cash equivalents of approximately $5.5 million. We currently estimate that we will use the net proceeds from this offering, together with $8.5 million from the sale of our 2014 notes in the first quarter of 2014 and our existing cash and cash equivalents, as follows:

- approximately $26.0 million to fund clinical development of CRLX101;
- approximately $10.0 million to fund research and development of CRLX301 and other product candidates; and
- the remainder for working capital and other general corporate purposes.

The expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our clinical development, the status of and results from clinical trials, any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our planned use of the net proceeds from this offering and our existing cash and cash equivalents described above, we estimate that such funds will be sufficient to enable us to fund our planned randomized Phase 2 clinical trial of CRLX101 in combination with Avastin in relapsed renal cell carcinoma, to support the ongoing CRLX101 investigator-sponsored trials, to fund our planned Phase 1 clinical trial of CRLX301 and to fund our operating expenses, debt service and capital expenditure requirements for at least the next 18 months. We do not expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to fund the completion of clinical development of any of our product candidates.

Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation instruments, including short-term, interest-bearing, investment-grade securities and U.S. government securities.

DIVIDEND POLICY

We have not declared or paid any cash dividends on our capital stock since our incorporation. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay any cash dividends to the holders of our common stock in the foreseeable future. Our ability to pay dividends on our common stock is prohibited by the covenants of our loan and security agreement with Lighthouse Capital Partners VI, L.P. and may be further restricted by the terms of any future indebtedness we may incur.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2013, on:

- an actual basis;
- a pro forma basis giving effect to (i) the automatic conversion of all outstanding shares of our preferred stock into 6,826,019 shares of common stock upon the closing of this offering, (ii) the issuance of 769,594 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 2013 convertible notes upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014, (iii) the issuance of 923,377 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014 and (iv) the conversion of our outstanding warrants to purchase 1,857,226 shares of our preferred stock to warrants to purchase 128,672 shares of common stock upon the closing of this offering; and
- a pro forma as adjusted basis to give further effect to our issuance and sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and the filing and effectiveness of a restated certificate of incorporation upon the closing of this offering.

You should read the following table in conjunction with our consolidated financial statements and the related notes, “Selected Consolidated Financing Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” appearing elsewhere in this prospectus.

	As of December 31, 2013		
(in thousands, except share and per share data)	**Actual**	**Pro Forma**	**Pro Forma As Adjusted**
Cash and cash equivalents	$ 5,488	$ 5,488	$ 67,710
Capitalization:			
Long-term debt (including current portion)	$ 6,258	$ 6,258	$ 6,258
Convertible notes	8,824	—	—
Warrant liability	928	—	—
Seed redeemable convertible preferred stock, par value $0.01 per share; 2,500,000 shares authorized, 2,500,000 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	2,000	—	—
Series A redeemable convertible preferred stock, par value $0.01 per share; 9,307,692 shares authorized, 9,307,692 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	12,100	—	—
Series B redeemable convertible preferred stock, par value $0.01 per share; 4,077,500 shares authorized, 3,562,500 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	7,125	—	—
Series B-1 redeemable convertible preferred stock, par value $0.01 per share; 5,000,000 shares authorized, 4,842,500 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	9,685	—	—
Series C redeemable convertible preferred stock, par value $0.01 per share; 33,310,787 shares authorized, 31,836,392 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	23,094	—	—

	As of December 31, 2013		
(in thousands, except share and per share data)	Actual	Pro Forma	Pro Forma As Adjusted
Series D redeemable convertible preferred stock, par value $0.01 per share; 34,698,793 shares authorized, 33,158,272 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	27,521	—	—
Common stock, par value $0.0001 per share; 132,000,000 shares authorized, 785,531 shares issued and outstanding actual, 8,366,375 shares outstanding pro forma and 14,304,520 shares outstanding pro forma as adjusted	—	1	1
Additional paid-in capital	4,140	95,650	157,109
Accumulated deficit	(98,439)	(98,439)	(98,439)
Total stockholder's deficit	(94,299)	(2,788)	58,671
Total capitalization	$ 3,236	$ 3,470	$ 64,929

The number of shares of our common stock to be issued upon the automatic conversion of all outstanding principal and accrued interest on our 2013 convertible notes and our 2014 convertible notes upon the closing of this offering depends in part on the initial public offering price of our common stock and the date on which this offering closes. As a result, the actual number of shares of common stock issued upon such conversion may differ from the number of shares set forth above. If the initial public offering price is equal to $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, (1) the outstanding principal and accrued interest on our 2013 convertible notes would convert into an aggregate of 769,594 shares of our common stock upon the closing of this offering and (2) the outstanding principal and accrued interest on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, or $9.30 per share, would convert into an aggregate of 923,377 shares of our common stock upon the closing of this offering, in each case assuming that the offering closes on April 15, 2014. A $1.00 increase in the assumed initial public offering price of $12.00 per share would decrease by 59,200 shares the aggregate number of shares of our common stock issuable upon the automatic conversion of the outstanding principal and interest accrued on our 2013 convertible notes upon the closing of this offering and would decrease by 71,030 shares the aggregate number of shares of our common stock issuable upon the automatic conversion of the outstanding principal and interest accrued on our 2014 convertible notes upon the closing of this offering. A $1.00 decrease in the assumed initial public offering price of $12.00 per share would increase by 69,962 shares the aggregate number of shares of our common stock issuable upon the automatic conversion of the outstanding principal and accrued interest on our 2013 convertible notes upon the closing of this offering and would increase by 83,942 shares the aggregate number of shares of our common stock issuable upon the automatic conversion of the outstanding principal and interest accrued on our 2014 convertible notes upon the closing of this offering.

A $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents and total stockholders' (deficit) equity by approximately $4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The table above does not include:

- 128,672 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 2013, at a weighted-average exercise price of $11.50 per share;
- 1,215,315 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2013, at a weighted-average exercise price of $4.84 per share;

- 139,076 shares of common stock reserved and available as of December 31, 2013 for future issuance under our 2007 Stock Incentive Plan, as amended; and
- 2,400,000 and 500,000 additional shares of our common stock that will be available for future issuance, as of the closing of this offering, under our 2014 stock incentive plan and our 2014 employee stock purchase plan, respectively.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share and the pro forma tangible book value per share of our common stock after this offering.

Our historical net tangible deficit as of December 31, 2013 was $(95.1) million, or $(121.04) per share of our common stock. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by 785,531 shares of our common stock outstanding as of December 31, 2013.

Our pro forma net tangible deficit as of December 31, 2013 was $(3.6) million, or $(0.43) per share of common stock. Pro forma net tangible book value per share represents the amount of our total tangible assets less our total liabilities, divided by the pro forma number of shares of our common stock outstanding on December 31, 2013, after giving effect to (i) the automatic conversion of all of our outstanding shares of preferred stock into shares of our common stock upon the closing of this offering, (ii) the issuance of 754,825 shares of common stock upon the conversion of all outstanding principal and accrued interest as of December 31, 2013 our 2013 convertible notes upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15 , 2014 and (iii) the reclassification of our preferred stock warrant liability to additional paid in capital, a component of stockholders (deficit) equity.

After giving effect to our issuance and sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, the issuance of 923,377 shares of common stock upon the conversion of all outstanding principal and interest on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014 and the issuance of 14,768 shares of common stock upon the conversion of accrued interest on our 2013 convertible notes for the period beginning January 1, 2014 to April 15, 2014, our pro forma as adjusted net tangible book value as of December 31, 2013 would have been $58.7 million, or $4.10 per share. This represents an immediate increase in pro forma net tangible book value per share of $4.53 to existing stockholders and immediate dilution of $7.90 in pro forma net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$12.00
Historical net tangible deficit per share as of December 31, 2013	$(121.04)	
Pro forma per share increase attributable to pro forma transactions described in preceding paragraphs	120.61	
Pro forma net tangible deficit per share as of December 31, 2013	(0.43)	
Increase per share attributable to the conversion of notes and accrued interest	0.96	
Increase per share attributable to sale of shares of common stock in this offering	3.57	
Pro forma as adjusted net tangible book value per share after this offering		$ 4.10
Dilution per share to new investors		$ 7.90

Each $1.00 increase in the assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, would increase our pro forma net tangible book value by approximately $4.7 million, the pro forma net tangible book value per share after this offering by

$0.37 per share and the dilution to investors in this offering by $0.63 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discount and offering expenses payable by us. Each $1.00 decrease in the assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, would decrease our pro forma net tangible book value by approximately $4.7 million, the pro forma net tangible book value per share after this offering by $0.36 per share and the dilution to investors in this offering by $0.64 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discount and offering expenses payable by us.

If the underwriters exercise their over-allotment option to purchase additional shares or if any additional shares are issued in connection with outstanding options, you will experience further dilution.

The following table summarizes, on a pro forma basis as of December 31, 2013, the total number of shares purchased from us, the total consideration paid, or to be paid, and the average price per share paid, or to be paid, by new investors in this offering at an assumed public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares Purchased		Total Consideration (Amounts in millions)		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	9,304,521	65%	$ 102.5	63%	$ 11.02
New investors	5,000,000	35%	60.0	37%	12.00
Total	14,304,521	100%	162.5	100%	

A $1.00 increase in the assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, would increase the total consideration paid by new investors by $5.0 million and increase the percentage of total consideration paid by new investors by approximately 2%, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. A $1.00 decrease in the assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, would decrease the total consideration paid by new investors by $5.0 million and decrease the percentage of total consideration paid by new investors by approximately 2%, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

The table above is based on actual shares of our common stock outstanding as of December 31, 2013 and 6,826,019 additional shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering and also reflects (1) the issuance of 769,594 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 2013 convertible notes upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014 and (2) the issuance of 923,377 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014.

The table above does not include:

- 128,672 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 2013, at a weighted-average exercise price of $11.50 per share;

- 1,215,315 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2013, at a weighted-average exercise price of $4.84 per share;
- 139,076 shares of common stock reserved and available as of December 31, 2013 for future issuance under our 2007 Stock Incentive Plan, as amended; and
- 2,400,000 and 500,000 additional shares of our common stock that will be available for future issuance, as of the closing of this offering, under our 2014 stock incentive plan and our 2014 employee stock purchase plan, respectively.

The number of shares of our common stock to be issued upon the automatic conversion of all outstanding principal and accrued interest on our 2013 convertible notes and our 2014 convertible notes upon the closing of this offering depends in part on the initial public offering price of our common stock and the date on which this offering is complete. As a result, the actual number of shares of common stock issued upon such conversion may differ from the number of shares set forth above.

If the underwriters exercise their option to purchase additional shares from us in full, the number of shares held by new investors will increase to 5,750,000, or 38% of the total number of shares of common stock outstanding after this offering, and the percentage of shares held by existing stockholders will decrease to 62% of the total shares outstanding.

Certain of our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to $18.0 million of shares of common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The foregoing discussion and tables do not reflect any potential purchases by these potential purchasers.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and the related notes appearing elsewhere in this prospectus. We have derived the consolidated statements of operations data for the years ended December 31, 2012 and 2013 and for the period from November 28, 2005 (date of incorporation) to December 31, 2013 (as we are a development stage company) and the consolidated balance sheet data at December 31, 2012 and 2013 from our audited consolidated financial statements appearing elsewhere in this prospectus. Our historical results for any prior period are not necessarily indicative of the results to be expected in any future period.

(in thousands, except share and per share data)	Years Ended December 31, 2012	Years Ended December 31, 2013	Period from November 28, 2005 (Date of Incorporation) to December 31, 2013
Consolidated Statement of Operations:			
Revenue	$ 625	$ 6	$ 1,669
Operating expenses:			
Research and development	15,807	9,700	67,042
General and administrative	6,393	6,166	31,570
Total operating expenses	22,200	15,866	98,612
Other income (expense):			
Interest income	2	2	684
Interest expense	(567)	(1,487)	(2,395)
Decrease in value of preferred stock warrant liability	39	202	215
Total other (expense)—net	(526)	(1,283)	(1,496)
Net loss	(22,101)	(17,143)	(98,439)
Accretion of redeemable convertible preferred stock	(73)	—	(694)
Net loss attributable to common stockholders	$ (22,174)	$ (17,143)	$ (99,133)
Net loss per share attributable to common stockholders:			
Basic and diluted(1)	$ (36.39)	$ (25.05)	$ (164.80)
Weighted-average common shares outstanding:			
Basic and diluted	609,344	684,330	601,547
Pro forma net loss per share attributable to common stockholders (unaudited):			
Basic and diluted(1)		$ (2.14)	
Pro forma weighted-average common shares outstanding (unaudited):			
Basic and diluted		7,883,204	

(in thousands)	As of December 31 2012	2013	Pro Forma (2)	Pro Forma As Adjusted (3)(4)
Consolidated Balance Sheet Data:				
Cash and cash equivalents	$ 16,707	$ 5,488	$ 5,488	$ 67,710
Total assets	$ 17,661	$ 6,827	$ 6,827	$ 68,286
Total liabilities	$ 13,949	$ 19,601	$ 9,615	$ 9,615
Redeemable convertible preferred stock	$ 83,751	$ 81,525	$ —	$ —
Common stock	$ —	$ —	$ 1	$ 1
Additional paid in capital	$ 1,257	$ 4,140	$ 95,650	$ 157,109
Accumulated deficit	$(81,296)	$(98,439)	$(98,439)	$ (98,439)
Total stockholders (deficit) equity	$(80,039)	$(94,299)	$ (2,788)	$ 58,671

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(1) See notes 2 and 3 within the notes to our consolidated financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net (loss) income per share applicable to common stockholders and pro forma basic and diluted net (loss) income per share applicable to common stockholders.

(2) The pro forma balance sheet data give effect to (i) the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 6,826,019 shares of common stock upon the closing of this offering, (ii) the issuance of 769,594 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 2013 convertible notes upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15 , 2014, (iii) the issuance of 923,377 shares of common stock upon the conversion of all outstanding principal and accrued interest on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014 and (iv) the conversion of our outstanding warrants to purchase 1,857,226 shares of our preferred stock into warrants to purchase 128,672 shares of common stock upon the closing of this offering.

(3) The pro forma as adjusted balance sheet data give effect to our issuance and sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(4) A $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total assets and total stockholders' (deficit) equity by approximately $4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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 consolidated financial statements and the related notes appearing elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, 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 prospectus 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. Our nanopharmaceutical product candidates consist of proprietary polymers that are covalently linked to anti-cancer therapeutics, or payloads. We believe these nanopharmaceuticals dynamically target tumors by exploiting the leakiness of new blood vessels in tumors as an entry portal into tumor tissue, followed by active uptake into tumor cells and the sustained release of the anti-cancer payload inside the tumor cells.

Our lead product candidate, CRLX101, is a dynamically tumor targeted nanopharmaceutical in Phase 2 clinical development and has the potential to address an unmet need where existing cancer therapies fail. We believe CRLX101, which contains camptothecin as its anti-cancer payload, is a potent, durable and combinable inhibitor of topoisomerase 1, or topo 1, and hypoxia inducible factor, or HIF. Clinical trials for CRLX101 have been conducted in multiple indications at several sites in over 200 patients. In clinical trials conducted to date, CRLX101 appears to be active and well tolerated as monotherapy and active and combinable with Avastin (bevacizumab). In addition, we believe CRLX101 may be combinable with other anti-cancer therapies. We are pursuing development of CRLX101 in combination with anti-cancer therapies in three ongoing clinical development programs:

- A combination trial with Avastin in Phase 2 in patients with relapsed renal cell carcinoma;
- A two-part clinical trial in Phase 2 in patients with relapsed ovarian cancer—consisting of a single-arm trial of CRLX101 as monotherapy and a single-arm combination trial with Avastin; and
- A combination trial with Xeloda (capecitabine) and radiotherapy in Phase 1b in patients with rectal cancer who are being treated through the administration of therapeutic agents prior to surgery. We refer to this form of treatment as neoadjuvant therapy, and we refer to patients who receive neoadjuvant therapy as patients with neoadjuvant rectal cancer.

CRLX301, the second product candidate from our dynamic tumor targeting platform, is a nanopharmaceutical with docetaxel as its anti-cancer payload. Based on observations in preclinical animal tumor models, we believe CRLX301 has the potential to enhance the clinical efficacy, achieve a higher therapeutic index and improve the adverse event profile of docetaxel. We intend to commence clinical trials of CRLX301 by the end of 2014.

In addition to CRLX101 and CRLX301, we have generated additional nanopharmaceuticals using our dynamic tumor targeting platform. We intend to pursue additional product candidate opportunities either by ourselves or in strategic partnerships with pharmaceutical companies to maximize value generation from our platform.

In 2011, we initiated an open-label, randomized Phase 2 clinical trial of CRLX101 as monotherapy in patients with advanced non-small cell lung cancer, or NSCLC, who had progressed through one or two prior regimens of chemotherapy. This Phase 2 clinical trial, or the NSCLC clinical trial, which enrolled 157 patients, 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. However, we observed clear evidence of activity for CRLX101 as measured by Response Evaluation Criteria in Solid Tumors, or RECIST, and observed progression free survival and overall survival comparable to the progression free survival and overall survival observed in approved cancer therapies in this setting. During 2012, the cost of the NSCLC clinical trial was a significant component of our research and development expense.

We have devoted substantially all of our resources to our drug discovery and development efforts, including conducting clinical trials for our product candidates, protecting our intellectual property and the general and administrative support of these operations. To date, 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 December 31, 2013, we have funded our operations primarily through $84.2 million in proceeds from the sale of shares of our convertible preferred stock, $10.0 million in proceeds from borrowings under our loan and security agreement with Lighthouse Capital Partners VI, L.P., or Lighthouse Capital, and $8.8 million in proceeds from our sale of convertible promissory notes.

We have never been profitable and have incurred significant operating losses since our incorporation. As of December 31, 2013, we had an accumulated deficit of $98.4 million. We incurred net losses of approximately $22.1 million for the year ended December 31, 2012 and $17.1 million for the year ended December 31, 2013.

We expect to continue to incur significant and increasing expenses and operating losses for the foreseeable future, as we attempt to advance our product candidates from discovery 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. We do not expect to generate revenue from product sales for at least the next several years, if ever. 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 2011, 2012 and 2013 from two material transfer agreements and a research agreement.

Research and Development Expenses

Research and development expense consists of costs incurred in connection with the discovery and development of our nanopharmaceutical platform and our product candidates. These expenses consist primarily of:

- employee-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, investigative sites that conduct our clinical trials and consultants that conduct a portion of our preclinical studies;

- expenses relating to scientific 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 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 seek to continue multiple clinical trials of our most advanced product candidate, CRLX101, initiate and continue clinical testing of 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. Expenses incurred prior to the acquisition of our cyclodextrin polymer containing nanopharmaceutical, or CDP, technology in mid-2009 have been reflected as the cost to develop our proprietary nanopharmaceutical platform in the period from November 28, 2005 (the date of our incorporation) to December 31, 2013, as these expenses were incurred prior to the establishment of the CRLX101 and CRLX301 programs. Below is an unaudited summary of our research and development expenses for the years ended December 31, 2012 and 2013 and the period from the date of our incorporation through December 31, 2013 (in thousands).

	Years Ended December 31,		**Period from November 28, 2005 (Date of Incorporation) to December 31, 2013**
	2012	**2013**	
CRLX101	$ 8,379	$4,655	$ 28,339
CRLX301	3,792	2,299	7,527
Nanopharmaceutical platform	2,618	2,007	26,449
Overhead	1,018	739	4,727
Total research and development expense	$15,807	$9,700	$ 67,042

The following summarizes our research and development programs.

CRLX101

We are supporting a Phase 1b/2 investigator-sponsored trial, or IST, of CRLX101 in combination with Avastin in patients with relapsed renal cell carcinoma, and we intend to commence a randomized, well-controlled Phase 2 clinical trial of CRLX101 in combination with Avastin in this indication in the second half of 2014. We are supporting a Phase 2 IST of CRLX101 as monotherapy in patients with relapsed ovarian cancer and a Phase 2 IST of CRLX101 in combination with Avastin in patients with relapsed platinum-resistant ovarian cancer.

Assuming positive results from the two ISTs in relapsed ovarian cancer, we expect to initiate, in 2015, a pivotal randomized clinical trial of CRLX101 in combination with Avastin in this indication. We are supporting a Phase 1b/2 IST of CRLX101 in combination with chemoradiotherapy, consisting of Xeloda and radiotherapy, in patients with neoadjuvant rectal cancer, and, assuming favorable results from this trial, we expect to commence a randomized, well-controlled Phase 2 clinical trial of CRLX101 in combination with chemoradiotherapy in this indication in 2015.

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 CLRX101, or the CRLX101 Agreement, we will be required to make regulatory and commercial milestone payments in an aggregate amount of up to $32.8 million to Calando upon the achievement of specified regulatory and commercial milestones. 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, depending on whether there is patent protection for CRLX101 at the time of the sale, as a percentage of worldwide net sales. 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 currently conducting preclinical studies of CRLX301 and intend to commence clinical trials by the end of 2014. We cannot accurately predict future research and development expenses for our CRLX301 program because such costs 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 the planned Phase 1 clinical trials and any future trials.

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 will be required to pay a $250,000 clinical development milestone to Calando when we initiate our Phase 1 clinical trial of CRLX301. We intend to initiate the Phase 1 clinical trial and pay this milestone by the end of 2014. We may also be required to make regulatory and commercial milestone payments in an aggregate amount of up to $17.8 million to Calando upon the achievement of specified regulatory and commercial milestones. 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, depending on whether there is patent protection for CRLX301 at the time of the sale, as a percentage of worldwide net sales. 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 and varies depending on the development stage of CRLX301 at the time that we first provide or receive draft terms of a license arrangement with the third party that results in a license agreement.

Nanopharmaceutical Pipeline

We expect that the expenses related to our nanopharmaceutical pipeline 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 nanopharmaceutical pipeline because such costs are dependent on a number of variables, including the success of preclinical studies on any such nanopharmaceuticals.

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

- the scope and rate of progress of our ongoing as well as any additional clinical trials;
- the scope, progress, results and costs of preclinical development, laboratory testing and other research and development activities;
- results from ongoing as well as any additional clinical trials;
- significant and changing government regulation;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain strategic partnerships, and the terms and success of those partnerships, if any, including the timing and amount of payments that we might receive from potential strategic partners;
- our ability to manufacture, market, commercialize and achieve market acceptance for any of our product candidates 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 a product candidate could mean a significant change in the cost and timing associated with the development of that product candidate. 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 completion of clinical development of a product candidate, 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 on the completion of clinical development.

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 product candidates. 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 success of each product candidate, as well as our ongoing assessment of the product candidate’s 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 product candidates.

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 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 product candidates;
- we expect our general and administrative expenses 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 product candidates in anticipation of commercial launch before we receive regulatory approval of a product candidate.

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 our debt facility with Lighthouse Capital.

Change in Fair Value of Preferred Stock Warrant Liability

The preferred stock warrant liability is associated with warrants to purchase shares of our preferred stock issued to lenders and investors. The change in fair value consists of the calculated change in value based upon the fair value of the underlying security at the end of each reporting period as calculated using the Black-Scholes option-pricing model.

Results of Operations

Comparison of Twelve Months Ended December 31, 2012 and 2013

The following table summarizes our consolidated results of operations for the years ended December 31, 2012 and 2013, together with the changes in those items in dollars and as a percentage (in thousands, except percentages):

	Years Ended December 31,		**Change**	
	2012	**2013**	**Dollar**	**%**
Revenue	$ 625	$ 6	$ (619)	*
Operating expenses:				
Research and development	15,807	9,700	(6,107)	(39)%
General and administrative	6,393	6,166	(227)	(4)%
Loss from operations	(21,575)	(15,860)	5,715	26%
Other income/(expense), net	(526)	(1,283)	(757)	*
Net loss	$ (22,101)	$ (17,143)	$ 4,958	22%

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* Not meaningful

Revenue. Revenue for the year ended December 31, 2012 was $0.6 million compared to $6,000 for the year ended December 31, 2013. We recorded revenue in 2012 and 2013 in connection with two material transfer agreements, each with a different pharmaceutical company. Pursuant to each of the agreements, we received payments in exchange for the pharmaceutical company's use of our proprietary technology for research purposes.

Research and development. The following table summarizes our research and development expense by program for the years ended December 31, 2012 and 2013, together with the change in spending by program in dollars and as a percentage (in thousands, except percentages):

	Years Ended December 31,		Change	
	2012	2013	Dollar	%
CRLX101	$ 8,379	$ 4,655	$(3,724)	(44)%
CRLX301	3,792	2,299	(1,493)	(39)%
Nanopharmaceutical platform	2,618	2,007	(611)	(23)%
Overhead	1,018	739	(279)	(27)%
Total research and development expense	$ 15,807	$ 9,700	$(6,107)	(39)%

Research and development expense for the year ended December 31, 2012 was $15.8 million compared to $9.7 million for the year ended December 31, 2013, a decrease of $6.1 million, or 39%. The decrease was reflected across all programs. The $3.7 million decrease in CRLX101 expense was primarily the result of winding down the NSCLC clinical trial, which was substantially completed in March 2013. Clinical trial expense decreased $2.1 million and contract manufacturing expense for clinical trial material decreased $1.6 million. The decrease in spending on the CRLX301 program in the year ended December 31, 2013 from the year ended December 31, 2012 was the result of our completion of development activities, such as investigational new drug, or IND, enabling studies and process development, early in 2013. We intend to advance CRLX301 into a Phase 1 clinical trial by the end of 2014. Expenses associated with our nanopharmaceutical platform decreased $0.6 million, mainly as a result of reduced staff in new discovery research as our primary emphasis shifted to the development of our product candidates. The $0.3 million overhead decrease was due mainly to a reduction in retainer-based advisory agreements and reduced depreciation expense.

General and administrative. General and administrative expense for the year ended December 31, 2012 was $6.4 million compared to $6.2 million for the year ended December 31, 2013, a decrease of $0.2 million, or 4%. The decrease was the result of a $0.4 million decrease in outside corporate and intellectual property legal expenses, offset by a $0.1 million increase in personnel costs and a $0.1 million increase in consulting expense.

Other income (expense), net. Other expense, net for the year ended December 31, 2012 was $(0.5) million compared to ($1.3) million net expense for the year ended December 31, 2013, an increased expense of $0.8 million. The increase in net expense primarily resulted from $0.9 million increase in recorded interest expense on our borrowings under our loan and security agreement with Lighthouse Capital. We entered into a loan and security agreement with Lighthouse Capital in December 2011 and borrowed $5.0 million in March 2012 and $5.0 million in August 2012. In addition, the adjustment to the fair value of our outstanding preferred stock warrants resulted in $0.2 million of other income for the year ended December 31, 2013 compared with $39,000 for the year ended December 31, 2012.

Liquidity and Capital Resources

From our incorporation through December 31, 2013, we have raised an aggregate of $103.0 million to fund our operations, of which $84.2 million was from the sale of preferred stock, $10.0 million was from borrowings under our loan and security agreement with Lighthouse Capital and $8.8 million was from the sale of convertible promissory notes. As of December 31, 2013, we had cash and cash equivalents of approximately $5.5 million.

Indebtedness

In 2011, we entered into a loan and security agreement, or the loan agreement, with Lighthouse Capital. The loan agreement 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. The loan agreement is secured by substantially all of our assets other than our intellectual property. We have also granted Lighthouse Capital 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. The loan agreement includes restrictive covenants that may restrict our ability to obtain further debt or equity financing. The aggregate principal amount outstanding accrues interest at an annual rate of 8.25% and is payable over 36 monthly payments beginning on December 1, 2012, with a one-time final payment of 6% of the original principal amount due on December 1, 2015. As of December 31, 2013, there was $6.7 million in principal amount outstanding under the loan agreement.

In 2013, we issued and sold convertible promissory notes, or our 2013 convertible notes, in an aggregate principal amount of $8.8 million to certain of our stockholders. Our 2013 convertible notes bear interest at an annual rate of 7% and are payable after one year upon demand made by the holders of at least 60% of the aggregate principal amount outstanding under the 2013 convertible notes. Upon closing of this offering, all principal and accrued interest under our 2013 convertible notes will convert into an aggregate of 769,594 shares of our common stock, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014.

In 2014, we issued and sold convertible promissory notes, or the 2014 convertible notes, in an aggregate principal amount of $8.5 million to certain of our stockholders and one additional purchaser. The 2014 convertible notes bear interest at an annual rate of 7% and are payable after one year upon demand made by the holders of at least 60% of the aggregate principal amount outstanding under the 2014 convertible notes. Upon closing of this offering, all principal and accrued interest under our 2014 convertible notes will convert into an aggregate of 923,377 shares of our common stock, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014. The principal and accrued interest under our 2014 convertible notes will convert at 77.5% of the initial public offering price.

Plan of Operations and Future Funding Requirements

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

We believe that the net proceeds from this offering, together with approximately $8.0 million of cash and cash equivalents as of February 28, 2014, and the additional $2.5 million of proceeds received in March 2014 through the issuance of the 2014 convertible notes, will fund our operating expenses, debt service and capital expenditure requirements for at least the next 18 months, which we expect will enable us to fund our planned randomized Phase 2 clinical trial of CRLX101 in combination with Avastin in relapsed renal cell carcinoma, to support the ongoing CRLX101 investigator-sponsored trials and to fund our planned Phase 1 clinical trial of CRLX301. We have based these estimates on assumptions that may prove to be wrong, and we may exhaust our capital resources sooner than we currently expect. In addition, the process of testing product candidates in clinical trials is costly, and the timing of progress in clinical trials is uncertain. Because our drug candidates are in various stages of clinical and preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability. Our future capital requirements will depend on many factors, including:

- the progress and results of our clinical trials of CRLX101;

- the progress and results of our clinical trials of CRLX301;
- our ability to manufacture sufficient supply of our product candidates and costs thereof;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other drug candidates;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution for any of our drug candidates for which we receive marketing approval;
- the number and development requirements of other drug candidates we pursue;
- our ability to enter into collaborative agreements and achieve milestones under those agreements;
- the revenue, if any, received from commercial sales of our drug candidates for which we receive marketing approval;
- 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; and
- the extent to which we acquire or in-license other products and technologies.

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. In 2014, we issued and sold an aggregate principal amount of $8.5 million of our 2014 convertible notes to certain of our existing stockholders and one additional purchaser. We expect our current cash, including proceeds from our 2014 convertible notes, and cash equivalents will enable us to fund our operations through at least the closing of the initial public offering process. 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):

	Years Ended December 31,		Period from November 28, 2005 (Date of Incorporation) to December 31,
	2012	2013	2013
Net cash (used in) operating activities	$ (21,005)	$ (16,614)	$ (90,652)
Net cash (used in) investing activities	$ (180)	$ (7)	$ (2,333)
Net cash provided by financing activities	$ 22,547	$ 5,402	$ 98,473
Net increase (decrease) in cash and cash equivalents	$ 1,362	$ (11,219)	$ 5,488

Net Cash Used in Operating Activities

The net use of cash in all periods 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 $21.0 million for the year ended December 31, 2012 compared with $16.6 million for the year ended December 31, 2013, a decrease of $4.4 million. The decrease primarily resulted from a $6.1 million decrease in research and development expense and $0.2 million decrease in general and administrative expense. These decreases were offset by a $0.7 million increase in interest payments on our debt facility with Lighthouse Capital, $0.6 million in collaboration revenue recorded in the year ended December 31, 2012 and $0.6 million resulting from net changes in the components of working capital.

Net Cash Used in Investing Activities

Net cash used in investing activities was $180,000 for the year ended December 31, 2012 compared to $7,000 for the year ended December 31, 2013. The decrease was primarily the result of additional research laboratory equipment, employee computers and office equipment and furniture purchased in the year ended December 31, 2012 compared to similar purchases in the year ended December 31, 2013.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $22.5 million during the year ended December 31, 2012 compared to $5.4 million during the year ended December 31, 2013. During the year ended December 31, 2013, we sold $8.8 million in convertible promissory notes and repaid indebtedness under the loan agreement with Lighthouse Capital in the amount of $3.1 million and we paid $0.4 million of debt issuance cost related to the convertible note issuance and this offering. In the year ended December 31, 2012, we sold preferred stock for net proceeds of $12.9 million, borrowed $10.0 million under our loan agreement with Lighthouse Capital and repaid indebtedness under the loan agreement in the amount of $0.4 million.

Contractual Obligations and Contingent Liabilities

The following summaries our significant contractual obligations as of December 31, 2013 (in thousands):

	Payments Due by Period ($)				
Contractual Obligations	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
Operating Lease Obligations(1)	1,338	610	728		—
Debt Obligations(2)	6,670	3,349	3,321	—	—

(1) Represents minimum future lease payments under our non-canceleable operating lease. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) Consists of payment obligations for principal and interest under our debt facility with Lighthouse Capital. As of December 31, 2013, we had $6.7 million in outstanding borrowings under the debt facility, bearing interest at 8.25%. Under the terms of the loan agreement governing the debt facility, we were 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 August 2012. The loan agreement is secured by substantially all of our assets other than our intellectual property. We have also granted Lighthouse Capital 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. The aggregate principal amount outstanding accrues interest at an annual rate of 8.25% and is payable over 36 monthly payments beginning on December 1, 2012, with a one-time final payment of 6% of the original principal amount due on December 1, 2015.

Milestone and royalty payments associated with our license agreements have not been included in the above table of contractual obligations as we cannot reasonably estimate if or when they will occur. Possible future payments under our intellectual property agreements include the following:

- Under the CRLX101 Agreement, we will be required to pay to Calando: (1) milestone payments in an aggregate amount of up to $32.8 million upon the achievement of certain development, regulatory and commercial milestones, (2) tiered royalty payments ranging from low- to mid-single digits, as a percentage of worldwide net sales, if we or one of our affiliates sells CRLX101 and (3) a percentage, ranging from the low- to mid-double digits, of any licensing or sublicensing income we receive from our license or sublicense of CRLX101.

- Under the Platform Agreement, we will be required to pay to Calando: (1) a $250,000 clinical development milestone to Calando when we initiate our Phase 1 clinical trial of CRLX301, (2) additional milestone payments in an aggregate amount of up to $17.8 million to Calando upon the achievement of certain regulatory and commercial milestones, (3) tiered royalty payments ranging from low- to mid-single digits, as a percentage of worldwide net sales, in the event we or one of our affiliates sells CRLX301 and (4) a percentage, in the low-double digits, of any licensing or sublicensing income we receive from our license or sublicense of CRLX301.
- Under our license agreement with the California Institute of Technology, or Caltech, we are obligated to pay Caltech (1) an annual minimum royalty of $10,000, (2) reimbursement for any costs it incurs to prosecute and maintain the patent rights licensed pursuant to the license agreement, subject to certain offsets and (3) certain amounts that Caltech would have been entitled to receive from Calando under its prior license agreement with Calando with respect to our sales of products licensed under the license agreement.
- Under our license agreement with The Research Foundation of State University of New York on behalf of University at Buffalo, or SUNY, we are obligated to pay SUNY (1) an escalating annual license maintenance fee, (2) development milestone payments not to exceed, in the aggregate, $100,000 and (3) royalties in the low single digits as a percentage of net sales of products covered by the patent rights licensed under the license agreement.
- Under our license agreement with the Massachusetts Institute of Technology, or MIT, we are obligated to pay MIT (1) an escalating annual license maintenance fee beginning in January 2015, (2) royalties at a low single digit percentage of net sales of products covered by the patent rights licensed pursuant to the license agreement and (3) a percentage, in the low double digits, of sublicense payments we receive from sublicenses of the patents licensed pursuant to the license agreement. None of our lead product candidates utilize technology covered by our license agreement with MIT.

In the course of our normal business operations, we also enter into agreements with contract service providers and others to assist in the performance of our research and development and manufacturing activities. As of December 31, 2013, we had open contracts and purchase orders with research institutions, contract research organizations, contract manufacturers and other clinical trial support vendors in the amount of approximately $4.9 million, of which we recorded approximately $1.0 million as accrued expenses in our consolidated financial statements. We will record the remaining $3.9 million as expenses in future periods, if and when the services under such contracts and purchase orders are delivered. We can elect to discontinue the work under these contacts and purchase orders at any time with notice, and such contracts and purchase orders do not contain minimum purchase obligations.

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.

Critical Accounting Policies and Use of Estimates

Our management’s discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstance, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

Our significant accounting policies are described in more detail in Note 2 of the notes to our consolidated financial statements appearing elsewhere in this prospectus. We believe the following accounting policies are critical to the judgments and estimates used in the preparation of the consolidated financial statements.

Accrued Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued clinical expenses include:

- fees paid to contract research organizations in connection with clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of clinical trial materials; and
- fees paid to vendors in connection with the preclinical development activities.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing the service fees, we consider the terms of each agreement, the time period over which the services will be performed and the level of effort required to complete the service. If the actual timing of the performance of the services or the level of effort varies from our estimate, we adjust the accrual accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. Based on our level of clinical trial expenses as of December 31, 2013, if our estimates are too high or too low by 5%, this may result in an adjustment to our accrued clinical trial expenses in future periods of approximately $30,000.

Preferred Stock Warrant Liability

As of December 31, 2013, we had outstanding warrants for the purchase of shares of our preferred stock. Freestanding warrants related to shares that are redeemable or contingently redeemable are classified as a liability on our consolidated balance sheet. We use the Black-Scholes option-pricing model to estimate the fair value of the warrants. Changes in the fair value of these warrants fluctuate with changes in the underlying assumptions in the Black-Scholes method and are recorded in our consolidated statements of operations. The significant assumptions include the risk-free interest rate, the estimated life of the warrant, volatility and the underlying value of our preferred stock.

Stock-Based Compensation

We issue stock-based awards to employees and non-employees in the form of stock options. We apply the fair value recognition provisions of the Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, *Compensation-Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and modifications to existing stock options, to be recognized in the consolidated statements of operations based on their fair values. We account for stock-based awards to non-employees in accordance with FASB ASC Topic 515-50, *Equity-Based Payments to Non-Employees*, which requires the fair value of the award to be re-measured at fair value as the award vests. We recognize the compensation expense of stock-based awards on a straight-line basis over the vesting period of the award for employees and non-employees. We have issued some performance-based grants where the vesting of the grant is tied to achievement of certain milestones, and, in these cases, the compensation expense is recognized when the milestone is met and the option is vested. Compensation expense related to our stock-based awards is subject to a number of estimates, including the estimated volatility and underlying fair value of our common stock, as well as the estimated life of the awards.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of our stock, (b) the expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. For these analyses, we have selected companies with comparable characteristics to ours, including enterprise value, risk profile and position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We have estimated the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the United States Treasury yield curve in effect during the period in which the options were granted.

We are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in our consolidated financial statements is based on awards that are ultimately expected to vest.

We have computed the fair value of employee stock options at date of grant using the following weighted-average assumptions:

	Years Ended December 31,	
	2012	2013
Expected volatility	77% - 79%	59% -79%
Expected term (in years)	6.00	6.00
Risk-free interest rate	0.83% - 1.12%	1.09% - 1.92%
Expected dividend yield	0.0%	0.0%

Stock-based compensation for employees and non-employees totaled approximately $0.5 million and $0.6 million for the years ended December 31, 2012 and 2013, respectively, allocated as outlined below (in thousands):

	Years Ended December 31, 2012	Years Ended December 31, 2013
Research and development	$ 187	$ 284
General and administrative	342	338
Total	$ 529	$ 622

As of December 31, 2013, we had $0.6 million of total unrecognized compensation expense, net of related forfeiture estimates, which is expected to be recognized over a weighted-average remaining vesting period of approximately 2.11 years. We expect our stock-based compensation expense for stock options and restricted stock granted to employees and non-employees to increase in future periods due to the potential increases in the value of our common stock and headcount.

Common Stock Valuation

The following table summarized by grant date the number of shares of common stock underlying stock options granted between January 1, 2012 and the date of this prospectus, as well as the associated per share exercise price and the estimated fair value per share of our common stock on the grant date:

Grant Dates	Number of Shares Underlying Options Granted	Exercise Price Per Share	Estimated Fair Value Per Share on Grant Date
January 25, 2012	252,974	$ 3.77	$ 3.77
February 6, 2012	12,504	$ 3.77	$ 3.77
March 7, 2012	1,379	$ 3.77	$ 3.77
June 5, 2012	10,340	$ 3.77	$ 3.77
September 19, 2012	4,308	$ 3.77	$ 3.77
December 7, 2012 – December 27, 2012	197,400	$ 3.92	$ 3.92
January 4, 2013	19,955	$ 3.92	$ 3.92
February 7, 2013	89,253	$ 3.92	$ 3.92
December 13, 2013	3,309	$ 7.54	$ 7.54
January 10, 2014 – January 27, 2014	159,608	$ 10.59	$ 10.59

We have historically granted stock options at exercise prices not less than the fair value of our common stock. As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors. We are a private company with no active public market for our common stock. Therefore, we have periodically determined for financial reporting purposes the estimated per share fair value of our common stock at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, or the Practice Aid. We performed these contemporaneous valuations as of December 31, 2011, December 1, 2012, September 30, 2013 and December 31, 2013. In conducting the contemporaneous valuations, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including our best estimate of our business condition, prospects and operating performance at each valuation date. Within the contemporaneous valuations performed, a range of factors, assumptions and methodologies were used. The significant factors included:

- the prices of our preferred stock sold to or exchanged between outside investors in arms' length transactions, and the rights, preferences and privileges of our preferred stock as compared to the rights of our common stock, including the liquidation preferences of our preferred stock;

- our results of operations, financial position and the status of our research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock given that we are a private company;
- our stage of development and business strategy and the material risks related to our business and industry;
- the achievement of enterprise milestones;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- any external market conditions affecting the life sciences and biotechnology industry sectors;
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, or a sale of our company, given prevailing market conditions;
- the state of the initial public offering market for similarly situated privately held biotechnology companies; and
- any recent contemporaneous valuations prepared by our board of directors and management in accordance with methodologies outlined in the Practice Aid.

The dates of our contemporaneous valuations have not always coincided with the dates of our stock-based compensation grants. In determining the exercise prices of the options granted, our board of directors considered, among other things, the most recent contemporaneous valuations of our common stock and our assessment of additional objective and subjective factors we believed were relevant as of the grant date. The additional factors considered when determining any changes in fair value between the most recent contemporaneous valuation and the grant dates included, when available, the prices paid in recent transactions involving our equity securities, as well as our stage of development, our operating and financial performance and current business conditions.

In September 2013, based on our review of overall market conditions and the improving market for biopharmaceutical initial public offerings, our board of directors determined that a significant shift was occurring with respect to the valuation that we could achieve in an initial public offering and directed us to begin preparation of a confidential draft registration statement for an initial public offering. We selected underwriters and held an organizational meeting in December 2013. We believe these events increased the probability of an early initial public offering scenario and therefore, in connection with the preparation of our consolidated financial statements, we re-assessed the fair value of our common stock for financial reporting purposes at interim dates between the contemporaneous valuations where there were stock option grants or modifications to existing grants. For these interim periods, we adjusted the fair value based on market conditions, progress made in our development programs and whether we achieved company milestones. A retrospective valuation was conducted as of May 31, 2013.

In April 2013, our board of directors approved the modification of stock options held by certain employees in connection with the reduction-in-force we implemented between April and August 2013. In exchange for a release of claims, vested stock options held as of termination by these employees were modified to extend the post-employment exercise period from ninety days to two years after the termination date. In addition, in June 2013, our board of directors approved accelerated vesting on certain stock options held by an executive officer included in the reduction-in-force. In December 2013, with the benefit of hindsight, and our belief that the probability of an initial public offering scenario had increased from April 2013, we conducted a retrospective valuation for our common stock as of May 31, 2013. The retrospective valuation for our common stock as of May 31, 2013 was used to record stock compensation expense for the modification on stock options for employees with termination dates in the second quarter of 2013. The contemporaneous valuation we conducted as of September 30, 2013, was used to record stock compensation expense for the modification on stock options for terminated employees with termination dates in the third quarter of 2013. In total, we recorded additional stock compensation expense of $0.1 million in connection with the stock option modifications.

Common Stock Valuation Methodologies

The contemporaneous and retrospective valuations discussed below were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its common stock. We generally used the market approach, in particular the guideline company and precedent transaction methodologies, based on inputs from comparable public companies' equity valuations and comparable acquisition transactions, to estimate the enterprise value of our company.

Methods Used to Allocate Our Enterprise Value to Classes of Securities

In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. The methods we considered consisted of the following:

- *Current Value Method.* Under the current value method, once the fair value of the enterprise is established, the value is allocated to the various series of preferred and common stock based on their respective seniority, liquidation preferences or conversion values, whichever is greatest.
- *Option Pricing Method.* Under the option pricing method, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options.
- *Probability-Weighted Expected Return Method, or PWERM.* The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

December 31, 2011 Contemporaneous Common Stock Valuation

In January 2012, we conducted a contemporaneous valuation of our common stock as of December 31, 2011, using the market approach, specifically the recent transactions method, to determine our enterprise value. As we had recently completed our Series D preferred stock financing in an arms' length transaction with investors, we determined this to be the best evidence of our value. We utilized the option pricing method to solve for the equity value that was consistent with the price paid by the Series D preferred investors. The option pricing method treats common stock and preferred stock as call options on the enterprise's value, with exercise prices based on the liquidation preference of the preferred stock. The common stock has value only if the funds available for distribution to shareholders exceed the value of the liquidation preference at the time of a liquidity event (for example, merger or sale), assuming the enterprise has funds available to make a liquidation preference meaningful and collectible by the shareholders. The common stock is modeled as a call option that gives its owner the right but not the obligation to buy the underlying enterprise value at a predetermined exercise price. In the model, the exercise price is based on a comparison with the enterprise value rather than, as in the case of a "regular" call option, a comparison with a per-share stock price. Thus, common stock is considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the preferred stock is liquidated. Typically option-pricing models such as the Black-Scholes model or a form of a lattice model (e.g. binomial) would be used to price the call option. The option pricing method considers the various terms of the stockholder agreements—including the level of seniority among the securities, dividend policy, conversion ratios and cash allocations—upon liquidation of the enterprise. In addition, the method implicitly considers the effect of the liquidation preference as of the future liquidation date, not as of the valuation date. In utilizing the recent transactions method, we utilized an option pricing method to estimate our equity value, which was consistent with the price paid for the Series D preferred stock acquired by investors on December 2, 2011.

In solving for the equity value implied by the Series D preferred stock financing we utilized the option pricing method and the key assumptions were as follows:

- Underlying equity value—Solved for the equity value that was consistent with the price paid for the Series D preferred shares.
- Volatility—We estimated volatility based on guideline publicly traded companies with a term consistent with the timeline to the liquidity event.
- Time to liquidity—We estimated a weighted-average time to a sale event of 2.00 years based on the projected time to significant clinical development events for our drug candidates.
- Risk-free interest rate—We determined the risk-free interest rate based on the yield of a United States Treasury bill with a maturity date closest to the estimated time to a sale event for our stockholders.
- Discounts for lack of control and marketability—The common stock options being granted represent an option to purchase a minority interest in us. As our capital structure is comprised of common and preferred shares, we considered the additional rights held by the holder of the preferred shares. The preferred shares possess certain rights not held by the common stockholders. These rights include, but are not limited to, drag-along rights and rights to appoint members of our board of directors. Additionally, as of December 31, 2011, we believed the most likely liquidity event was a sale. Because we are a privately-held company, shares of our common stock are highly illiquid and, as such, warrant a discount in value from their estimated "marketable" price. In assessing the discount, we used legal guidelines from United States Tax Court cases regarding privately-held business valuations, fundamental business factors and empirical studies on the discount for lack of marketability. We corroborated the discount based on the value of a put option compared to the value of common stock using a Black-Scholes option-pricing model. We also considered that our preferred stock has rights that our common stock does not have, including anti-dilution protection, redemption rights, protective provisions in our certificate of incorporation and rights to participate in future rounds of financing. Our preferred stockholders have control and influence over the enterprise, which provides them with the optionality over future liquidity, financing and other decisions that the common stock option holders do not control. As a result of these factors, we applied an aggregate 20% discount for lack of control and marketability.

The resulting value, which represented the estimated fair value of our common stock as of December 31, 2011, was $3.77 per share.

Stock Options Granted from January 25, 2012 to September 19, 2012

Our board of directors granted stock options on January 25, 2012, February 6, 2012, March 7, 2012, June 5, 2012 and September 19, 2012, each having an exercise price of $3.77 per share, which our board of directors determined to be the fair value of our common stock on each grant date. In addition to the objective and subjective factors discussed above, our board of directors considered input from management and the valuation as of December 31, 2011 in estimating the fair value of our common stock. Our board of directors determined that no significant events or other circumstances had occurred between December 31, 2011 and September 19, 2012 that would indicate there was a change in the fair value of our common stock. Moreover, during the period from December 31, 2011 to the date of the September 2012 awards, overall market conditions, and particularly the market for biopharmaceutical initial public offerings, were not promising. Based on these factors, our board of directors determined that the fair value of our common stock on each of these dates of grant was $3.77 per share.

December 1, 2012 Contemporaneous Common Stock Valuation

In December 2012, we conducted a contemporaneous valuation of our common stock as of December 1, 2012, using the market approach, specifically the recent transactions method, to determine our enterprise value.

Our selection of the market approach was based on the recent closing of an extension of the Series D preferred stock financing. We utilized the option pricing method to solve for the equity value which was consistent with the price paid by the Series D preferred investors on November 30, 2012.

In solving for the equity value implied by the Series D preferred stock financing we utilized the option pricing method and the key assumptions were as follows:

- Underlying equity value—Solved for the equity value that was consistent with the price paid for the Series D preferred shares.
- Volatility—We estimated volatility based on guideline publicly traded companies with a term consistent with the timeline to the liquidity event.
- Time to liquidity—We estimated a weighted-average time to a sale event of 2.50 years based on the projected time to significant clinical development events for our drug candidates.
- Risk-free interest rate—We determined the risk-free interest rate based on the yield of a United States Treasury bill with a maturity date closest to the estimated time to a sale event for our stockholders.
- Discounts for lack of marketability—We applied an aggregate 20% discount for lack of control and lack of marketability.

The estimated per share value of our common stock calculated in our valuation as of December 1, 2012 of $3.92 per share increased from the December 31, 2011 valuation of $3.77 per share primarily due to the following reasons:

- Second closing of our Series D preferred stock financing occurred on November 30, 2012; and
- NASDAQ Biotechnology Index increased 33% during the period.

These positive factors were partially offset by an increased timing to a liquidity event as a result of delays in obtaining final data from the NSCLC clinical trial.

Stock Options Granted from December 7, 2012 to February 3, 2013

Our board of directors granted stock options on December 7, 2012, December 19, 2012, December 27, 2012, January 4, 2013 and February 7, 2013, each having an exercise price of $3.92 per share, which our board of directors determined to be the fair value of our common stock on each grant date. In addition to the objective and subjective factors discussed above, our board of directors considered input from management and the valuation as of December 1, 2012 in estimating the fair value of our common stock. Given that we were operating within plan and there were no significant milestones attained in our clinical development program at each of the grant dates, our board of directors determined that no significant events or other circumstances had occurred between December 1, 2012 and February 3, 2013 that would indicate there was a change in the fair value of our common stock during that period.

May 31, 2013 Retrospective Common Stock Valuation

In December 2013, we conducted a retrospective valuation of our common stock as of May 31, 2013, using the hybrid method to value our common stock. Specifically, we used two market approaches, the recent transactions method and guideline initial public offering transactions, and a third scenario, sale below the liquidation preference with no value to the common stock, to estimate the value of our equity. In utilizing the recent transactions method, we utilized the option pricing method to estimate our equity value, which was consistent with the price paid for the Series D preferred shares by investors. In addition, we utilized a direct waterfall analysis to allocate the value to the respective share classes under the guideline initial public offering transactions method. Under the sale below the liquidation preference there is no value allocated to the common stock. In each case, we applied probability weightings to the various methodologies based upon our assessment of our prospects of a sale or merger transaction, an initial public offering or a sale below the liquidation preference.

For the retrospective valuation at May 31, 2013, we used the recent transactions method and the guideline initial public offering method to determine the value of our equity under the sale or merger and initial public offering scenarios. The recent transaction method was used to determine our value under a possible sale transaction and the guideline initial public offering method was used to estimate our equity value under the potential initial public offering scenario. There is no value allocated to the common stock under the sale below liquidation preference scenario. The specific facts and circumstances considered by our board of directors in assessing these key valuation assumptions included those noted in the following table:

May 31, 2013 Major Assumptions	Initial Public Offering	Option Pricing Method	Sale Below Liquidation Preference
Probability of scenario	25%	65%	10%
Discount for marketability	10%	10%	N/A
Timeline to liquidity	0.92 yrs	1.75 yrs	N/A
Discount rate—common stock	30%	N/A	N/A
Estimated per share fair value of common stock—before discounts	$13.35	$4.50	$ 0.00

In applying the market approach to estimate our future enterprise value under the initial public offering scenario, as described above, it was assumed that a liquidity event would occur in 0.92 years. Given our development pipeline and the status of our clinical trials, as of the valuation date the selected enterprise value in the initial public offering scenario was based on the pre-money initial public offering market data for transactions between the low and the 25th percentile of the observed range. The selected enterprise value contemplated our stage of development, amount of capital raised, depth of clinical candidates and number of partnerships and collaborations in comparison to the initial public offering transactions.

In applying the market approach to estimate our aggregate future enterprise value under the option pricing method scenario, as described above, it was assumed that a liquidity event would occur in 1.75 years. The selected enterprise value utilized in the option pricing method scenario was based on the recent Series D preferred stock financing. The investors paid $0.83 per share for the Series D preferred stock. We used the back-solve method, a form of the market approach that derives the implied value for one type of equity security from a contemporaneous transaction involving another type of equity security.

As noted above, under the sale below liquidation preference scenario, there is no value allocated to the common stock.

We applied a discount for lack of marketability of 10% under the initial public offering and option pricing method scenarios. We assessed the probabilities of each transaction and assigned a 25% weighting to the initial public offering scenario, 65% to the option pricing method scenario and 10% to the sale below liquidation preference based on our assessment of our development pipeline and market conditions. The resulting value, which represented the estimated fair value of our common stock as of May 31, 2013, was $5.66 per share.

The estimated per share fair value of our common stock calculated in our valuation as of May 31, 2013 of $5.66 per share increased from the December 1, 2012 valuation of $3.92 per share primarily due to the following factors:

- Timing to a prospective liquidity event had decreased since December 1, 2012;
- Increased likelihood of an initial public offering;
- Improved capital market conditions for biotechnology companies, as evidenced by a recent increase in the number of public offerings and their initial public offering valuations;

- Encouraging preliminary results from the Phase 2 IST of CRLX101 as monotherapy in patients with relapsed ovarian cancer; and
- the NASDAQ Biotechnology Index increased 30% during the period.

Stock Option Modifications in April through June 2013

In April 2013, our board of directors approved the modification of stock options to purchase 90,941 shares of our common stock held by certain terminated employees. The modifications extended the post-employment period during which the terminated employees could exercise such options and accelerated vesting for one terminated executive officer. We used the May 31, 2013 retrospective valuation to value the modifications, and accordingly, in connection with the modifications we recorded stock compensation expense of $92,000.

September 30, 2013 Contemporaneous Common Stock Valuation

In October 2013, we conducted a contemporaneous valuation of our common stock as of September 30, 2013, using the hybrid method to value our common stock. Specifically, we used two market approaches, the recent transactions method and guideline initial public offering transactions, and a third scenario, sale below the liquidation preference with no value to the common stock, to estimate the value of our equity. In utilizing the recent transactions method, we utilized an option pricing method to estimate our equity value. We had recently completed a convertible bridge debt financing in August 2013. The notes issued in the debt financing are convertible into the equity securities of the next qualified financing round or into Series D preferred shares. In utilizing the recent transactions method, we utilized the option pricing method to estimate our equity value, which is based on the price at which the notes would convert into Series D preferred shares. In addition, we utilized a direct waterfall analysis to allocate the value to the respective shares classes under the guideline initial public offering transactions method. Under the sale below the liquidation preference scenario there is no value allocated to the common stock. In each case, we applied probability weightings to the various methodologies based upon our assessment of our prospects of a sale or merger transaction, an initial public offering or the sale below the liquidation preference.

For the contemporaneous valuation at September 30, 2013, we used the recent transactions method and the guideline initial public offering method to determine the value of our equity under the sale or merger and initial public offering scenarios. The recent transaction method was used to determine our value under a possible sale transaction and the guideline initial public offering method was used to estimate the equity value under the potential initial public offering scenario. There is no value allocated to the common stock under the sale below liquidation preference scenario. The specific facts and circumstances considered by our board of directors in assessing these key valuation assumptions included those noted in the following table:

September 30, 2013 Major Assumptions	Initial Public Offering	Option Pricing Method	Sale Below Liquidation Preference
Probability of scenario	50%	40%	10%
Discount for marketability	10%	10%	N/A
Timeline to liquidity	0.58 yrs	1.50 yrs	N/A
Discount rate—common stock	30%	N/A	N/A
Estimated per share fair value of common stock—before discounts	$ 13.35	$ 4.21	$ 0.00

In applying the market approach to estimate our future enterprise value under the initial public offering exit scenario, as described above, it was assumed that a liquidity event would occur in 0.58 years. Given our development pipeline and the status of our clinical trials, as of the valuation date the selected enterprise value in the initial public offering scenario was based on the pre-money initial public offering market data for transactions between the low and the 25th percentile of the observed range. The selected enterprise value contemplated our stage of development, amount of capital raised, depth of clinical candidates and number of partnerships and collaborations in comparison to the initial public offering transactions.

In applying the market approach to estimate our aggregate future enterprise value under the option pricing method scenario, as described above, it was assumed that a liquidity event would occur in 1.50 years. The selected enterprise value utilized in the option pricing method scenario was based on the recent convertible bridge note financing. The bridge note investors may convert the debt at $0.83 per share for a share of Series D preferred stock. We used the back-solve method to determine our equity.

As noted above, under the sale below liquidation preference scenario there is no value allocated to the common stock.

We applied a discount for lack of marketability of 10% under the initial public offering and option pricing method scenarios. We assessed the probabilities of each transaction and assigned a 50% weighting to the initial public offering scenario, 40% to the option pricing method scenario and 10% to the sale below liquidation preference scenario based on our assessment of our development pipeline and market conditions. The resulting value, which represented the estimated fair value of our common stock as of September 30, 2013, was $7.54 per share.

The estimated per share fair value of our common stock calculated in our valuation as of September 30, 2013 of $7.54 per share increased from the retrospective May 31, 2013 valuation of $4.42 per share primarily due to the following factors:

- Timing to a prospective liquidity event had decreased since May 31, 2013;
- Increased likelihood of an initial public offering;
- Improved capital market conditions for biotechnology companies as evidenced by a recent increase in the number of public offerings and their initial public offering valuations;
- Detail analysis of the NSCLC clinical trial provided evidence of activity for CRLX101 as measured by RECIST, and progression free survival and overall survival in the treatment arm of the study;
- Encouraging early data from the Phase 1b/2 IST of CRLX101 in combination with Avastin in patients with relapsed renal cell carcinoma, and the identification of the maximum tolerated dose for CLRX101 when administered in combination with Avastin in this indication;
- Encouraging early data in the Phase 2 IST of CRLX101 in combination with Avastin in patients with relapsed ovarian cancer, and we confirmed our intention to begin a trial administering CRLX101 in combination with Avastin for platinum-resistant ovarian cancer patients, based on maximum tolerated dose identified in the renal cell carcinoma trial; and
- NASDAQ Biotechnology Index increased 17% during the period.

Stock Options Granted on December 13, 2013

Our board of directors granted stock options on December 13, 2013 having an exercise price of $7.54 per share, which our board of directors determined to be the fair value of our common stock on each grant date. The per share exercise price determined by our board of directors was supported by the September 30, 2013 valuation, as described more fully above, along with input from management. Our board of directors believed that this was appropriate as we had not selected bankers for an initial public offering, there were no changes to our operating plan and there were no significant milestones completed since September 30, 2013 that would indicate there was a change in the fair value of our common stock.

Stock Option Modifications in July through August 2013

We used the September 30, 2013 contemporaneous valuation to record stock compensation expense of $14,000 in connection with modifications to stock options held by employees who were terminated in July and

August 2013. These modifications, which were approved by our board of directors in April 2013, extended the post-employment period during which the terminated employees could exercise stock options that were vested at their respective termination dates.

December 31, 2013 Common Stock Valuation

For the December 31, 2013 contemporaneous valuation, we utilized the hybrid method to value our common stock. Specifically, we used two market approaches, the recent transactions method and guideline initial public offering transactions, and a third scenario, sale below the liquidation preference with no value to the common stock, to estimate the value of our equity. In utilizing the recent transactions method, we utilized an option pricing method to estimate our equity value. We recently completed a convertible bridge debt financing in August 2013. The notes issued in the bridge debt financing are convertible into the equity securities of the next qualified financing round or into Series D preferred shares. In utilizing the recent transactions method, we utilized the option pricing method to estimate our equity value, which was consistent with the price at which the notes issued in the debt financing would convert into Series D preferred shares. In addition, we utilized a direct waterfall analysis to allocate value to the respective shares classes under the guideline initial public offering transactions method. Under the sale below the liquidation preference scenario, there is no value allocated to the common stock. In each case, we applied probability weightings to the various methodologies based upon our assessment of our prospects of a sale or merger transaction or an initial public offering or the sale below the liquidation preference of our common stock.

For the contemporaneous valuation at December 31, 2013, we used the recent transactions method and the guideline initial public offering method to determine the value of our equity under the sale or merger and initial public offering scenarios. The recent transaction method was used to determine our value under a possible sale transaction and the guideline initial public offering method was used to estimate the equity value under the potential initial public offering scenario. There is no value allocated to the common stock under the sale below liquidation preference scenario. The specific facts and circumstances considered by our board of directors in assessing these key valuation assumptions included those noted in the following table

December 31, 2013 Major Assumptions	Initial Public Offering	Option Pricing Method	Sale Below Liquidation Preference
Probability of scenario	75%	20%	5%
Discount for marketability	10%	10%	N/A
Timeline to liquidity	0.33 yrs	1.50 yrs	N/A
Discount rate—common stock	25%	N/A	N/A
Estimated per share fair value of common stock—before discounts	$ 14.51	$ 4.21	$ 0.00

In applying the market approach to estimate our future enterprise value under the initial public offering scenario, as described above, it was assumed that a liquidity event would occur in 0.33 years. Given our development pipeline and the status of our clinical trials, as of the valuation date the selected enterprise value in the initial public offering scenario was based on the pre-money initial public offering market data for transactions between the low and the 25th percentile of the observed range. The selected enterprise value contemplated our stage of development, amount of capital raised, depth of clinical candidates and number of partnerships/collaborations in comparison to the initial public offering transactions.

In applying the market approach to estimate our aggregate future enterprise value under the option pricing method scenario, as described above, it was assumed that a liquidity event would occur in 1.50 years. The selected enterprise value utilized in the option pricing method scenario was based on the recent convertible bridge note financing. The bridge note investors may convert the debt at $0.83 per share for a share Series D preferred Stock. We used the back-solve method to determine our equity.

As noted above, under the sale below liquidation preference scenario there is no value allocated to the common stock.

We applied a discount for lack of marketability of 10% under the initial public offering and option pricing method scenarios. We assessed the probabilities of each transaction and assigned a 75% weighting to the initial public offering scenario, 20% to the option pricing method scenario and 5% to the sale below liquidation preference scenario based on our assessment of our development pipeline and market conditions. The resulting value, which represented the estimated fair value of our common stock as of December 31, 2013, was $10.59 per share.

The estimated per share fair value of our common stock calculated in our valuation as of December 31, 2013 of $10.59 per share increased from the September 30, 2013 valuation of $7.54 per share primarily due to the following factors:

- Timing to a prospective liquidity event has decreased since September 30, 2013;
- Increased likelihood of an initial public offering;
- Improved capital market conditions for biotechnology companies as evidenced by a recent increase in the number of public offerings and their initial public offering valuations;
- Investment bankers selected to lead the initial public offering;
- Initial public offering organizational meeting was held in December 2013; and
- NASDAQ Biotechnology Index increased 8% during the period.

Stock Options Granted in January 2014

Our board of directors granted stock options on January 10, 2014, January 15, 2014, January 16, 2014, January 22, 2014 and January 27, 2014, each having an exercise price of $10.59 per share, which our board of directors determined to be the fair value of our common stock on each grant date. In addition to the objective and subjective factors discussed above, our board of directors considered input from management and the valuation as of December 31, 2013 in estimating the fair value of our common stock. Given we had not yet submitted a registration statement for an initial public offering and there were no significant changes to our operating plan, our board of directors determined that no significant events or other circumstances had occurred between December 31, 2013 and January 27, 2014 that would indicate there was a change in the fair value of our common stock during that period.

Initial Public Offering Price Range

We and our underwriters determined the price range for this offering, as set forth on the cover page of this prospectus. The midpoint of the price range is $12.00 per share. In comparison, on January 27, 2014, we granted options with an exercise price of $10.59 per share, which was our estimate of the fair value of our common stock as of such date. We note that, as is typical in initial public offerings, the price range for this offering was not derived using a formal determination of fair value, but was determined by negotiation between us and the underwriters. Among the factors that were considered in setting this range were our future prospects and those of our industry in general, our financial and operating information in recent periods, the market prices of securities of companies engaged in activities similar to ours and general conditions in the public capital markets.

At the time option awards were last made, our underwriters had not yet communicated to us the definitive proposed price range for this offering. Specifically, we believe that the difference between the fair value of our common stock as of January 27, 2014 and the midpoint of the estimated price range for this offering is primarily the result of the following factors:

- The estimated price range for this offering necessarily assumes that this offering has occurred, a public market for our common stock has been created and that our preferred stock converted into common stock in connection with this offering, and therefore excludes any discount for lack of marketability of our common stock.

- Our preferred stock currently has substantial economic rights and preferences over our common stock. Upon the closing of this offering, all outstanding shares of our preferred stock will convert into common stock, thus eliminating the superior rights and preferences of our preferred stock as compared to our common stock.
- The proceeds of a successful initial public offering would substantially strengthen our balance sheet by increasing our cash resources. In addition, the completion of this offering would provide us with more ready access to the public company debt and equity markets. These projected improvements in our financial position influenced the increased common stock valuation indicated by the midpoint of the estimated price range shown on the cover of this prospectus.

Recent Accounting Pronouncements

From time to time, new pronouncements are issued by the FASB or other standard setting bodies that may have an impact on our accounting and reporting. We believe that such recently issued accounting pronouncements and other authoritative guidance for which the effective date is in the future either will not have an impact on our accounting or reporting or that such impact will not be material to our financial position, results of operations, and cash flows when implemented.

JOBS Act

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- reduced disclosure about our executive compensation arrangements;
- exemption from the non-binding advisory votes on executive compensation, including golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal controls over financial reporting.

Generally, we may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1 billion in annual revenue, we have more than $700 million in market value of our stock held by non-affiliates or we issue more than $1 billion of non-convertible debt over a three-year period. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of certain reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, the JOBS Act 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 will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2013, we had cash and cash equivalents of approximately $5.5 million, consisting primarily of investments in United States Treasuries 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.

BUSINESS

Overview

We are a clinical-stage oncology-focused company applying our proprietary dynamic tumor targeting platform to develop differentiated therapies. Our nanopharmaceutical product candidates consist of proprietary polymers that are covalently linked to anti-cancer therapeutics, or payloads. We believe these nanopharmaceuticals dynamically target tumors by exploiting the leakiness of new blood vessels in tumors as an entry portal into tumor tissue, followed by active uptake into tumor cells and the sustained release of the anti-cancer payload inside the tumor cells.

Our lead product candidate, CRLX101, is a dynamically tumor targeted nanopharmaceutical in Phase 2 clinical development and has the potential to address an unmet need where existing cancer therapies fail. We believe CRLX101, which contains camptothecin as its anti-cancer payload, is a potent, durable and combinable inhibitor of topoisomerase 1, or topo 1, a commercially validated cancer target, and hypoxia inducible factor, or HIF, a novel target of increasing interest in cancer research. Recent research suggests that HIF-la is a master regulator of multiple cancer cell survival pathways. Clinical trials for CRLX101 have been conducted in multiple indications at several sites in over 200 patients. In clinical trials conducted to date, CRLX101 appears to be active and well tolerated as monotherapy and active and combinable with Avastin (bevacizumab), a leading anti-cancer drug. In addition, we believe CRLX101 may be combinable with other anti-cancer therapies. We are pursuing development of CRLX101 in combination with anti-cancer therapies in three ongoing clinical development programs:

- A combination trial with Avastin in Phase 2 in patients with relapsed renal cell carcinoma;
- A two-part clinical trial in Phase 2 in patients with relapsed ovarian cancer—consisting of a single-arm trial of CRLX101 as monotherapy and a single-arm combination trial with Avastin; and
- A combination trial with Xeloda (capecitabine), which is a leading anti-cancer drug, and radiotherapy in Phase 1b in patients with rectal cancer who are being treated through the administration of therapeutic agents prior to surgery. We refer to this form of treatment as neoadjuvant therapy, and we refer to patients who receive neoadjuvant therapy as patients with neoadjuvant rectal cancer.

CRLX301, the second product candidate from our dynamic tumor targeting platform, is a nanopharmaceutical with docetaxel, a microtubule stabilizer, as its anti-cancer payload. Based on observations in preclinical animal tumor models, we believe CRLX301 has the potential to enhance the clinical efficacy, achieve a higher therapeutic index and improve the adverse event profile of Taxotere® (docetaxel). We intend to commence clinical trials of CRLX301 by the end of 2014.

In addition to CRLX101 and CRLX301, we have generated additional nanopharmaceuticals using our dynamic tumor targeting platform. We intend to pursue additional product candidate opportunities either by ourselves or in strategic partnerships with pharmaceutical companies to maximize value generation from our platform.

Our nanopharmaceuticals are polymer-based nanoparticles that are covalently linked to anti-cancer payloads. These nanopharmaceuticals form particulate structures that, we believe, dynamically target tumors in a three-step process that differentiates our nanopharmaceuticals from other nanopharmaceutical approaches. First, our nanopharmaceuticals exploit the leakiness of new blood vessels in tumors as an entry portal into tumor tissue. Second, our nanopharmaceuticals are actively taken up by tumor cells and, due to their size, our nanopharmaceuticals are not easily removed from cancer cells. Third, our nanopharmaceuticals provide sustained release of the anti-cancer payload inside the tumor cells. We believe these properties may result in improved efficacy by prolonging drug exposure in tumor cells, thus providing for an improved therapeutic index as compared to the anti-cancer payload alone.

Due to the dynamic tumor targeting of CRLX101 and the resulting sustained release of its anti-cancer payload, camptothecin, we believe CRLX101 achieves durable inhibition of topo 1, a commercially validated cancer target, and HIF, in particular HIF-la, an emerging target that recent research suggests is a master regulator of multiple cancer cell survival pathways. Camptothecin is an inhibitor of topo 1 and HIF-la and has shown evidence of strong anti-cancer activity in preclinical tumor models. However, clinical development of camptothecin was discontinued due to unacceptable toxicities. As a result, camptothecin has never been approved for use by the U.S. Food and Drug Administration, or the FDA, or any other regulatory agency. CRLX101 permits the dynamic targeting of camptothecin to tumor cells without causing unacceptable toxicities. In preclinical tumor models, CRLX101 as monotherapy outperformed commercial drug comparators. Moreover, CRLX101 appears to be combinable with other drugs and, in preclinical tumor models, demonstrated additive or synergistic properties when combined with commercial cancer drugs such as Taxol® (paclitaxel) and Platinol® (cisplatin). In preclinical tumor models, CRLX101 also has demonstrated synergy with vascular endothelial growth factor, or VEGF, inhibitors, such as Avastin, Zaltrap® (ziv-aflibercept) and Votrient® (pazopanib), and with radiotherapy. We hold issued patents in the United States, Japan and Europe covering the composition of matter of CRLX101 that expire in 2023 and 2024, excluding any potential patent term extension.

Due to the potentially broad applicability of our dynamic tumor targeting platform and CRLX101's apparently favorable adverse event profile observed to date, we believe CRLX101 may have significant clinical utility in several cancer indications, particularly in combination with cancer therapies and with radiotherapy. We are supporting investigator-sponsored Phase 1 and Phase 2 clinical trials of CRLX101 being conducted by leading academic medical centers in the United States. In collaboration with the investigators in these trials, our focus is on tumor types where HIF is up-regulated, topo 1 inhibition is desirable and drug combinations with CRLX101 can be pursued.

Based on CRLX101's inhibition of topo 1 and HIF, as well as its potential synergy with other anti-cancer therapies, we are currently focusing our CRLX101 clinical development program on combinations with cancer therapies in three tumor types: relapsed renal cell carcinoma in combination with Avastin; relapsed ovarian cancer in combination with Avastin; and neoadjuvant rectal cancer in combination with Xeloda plus radiotherapy. The CRLX101 clinical development program includes:

- *Relapsed renal cell carcinoma:* A Phase 1b/2 open-label investigator sponsored trial, or IST, of CRLX101 in combination with Avastin in patients with relapsed renal cell carcinoma is being conducted at the University of Pennsylvania and is expected to expand to Thomas Jefferson University. Based on preliminary results from this trial, we believe that the combination of CRLX101 and Avastin may provide therapeutic benefits to relapsed renal cell carcinoma patients. Specifically, Response Evaluation Criteria in Solid Tumors, or RECIST, responses, as well as encouraging progression free survival, have been achieved in several patients. We believe that the therapeutic benefits observed to date in the trial are due to CRLX101's synergy with Avastin and the resulting durable inhibition of HIF, topo 1 and VEGF. We intend to commence a randomized, well-controlled Phase 2 clinical trial of CRLX101 in combination with Avastin in the second half of 2014.
- *Relapsed ovarian cancer:* A two-part Phase 2 open-label IST of CRLX101 in patients with relapsed ovarian cancer is being conducted at Massachusetts General Hospital and affiliated Harvard teaching hospitals. The first part of the trial, a single-arm trial of CRLX101 as monotherapy, has completed enrollment and met its primary efficacy endpoint. Platinum-resistant ovarian cancer patients are being enrolled in the second part, a single-arm combination trial of CRLX101 and Avastin. Assuming positive results from the second part of the trial and adequate additional funding, we expect to initiate a randomized pivotal clinical trial of CRLX101 in combination with Avastin in relapsed platinum-resistant ovarian cancer in 2015.
- *Neoadjuvant rectal cancer:* A Phase 1b/2 open-label IST of CRLX101 in combination with chemoradiotherapy, consisting of Xeloda and radiotherapy, in patients with neoadjuvant rectal cancer is being conducted at the University of North Carolina at Chapel Hill and is expected to expand to the

University of Indiana and Wake Forest University. Assuming favorable results from this Phase 1b/2 trial and adequate additional funding , we expect to commence a randomized, well-controlled Phase 2 clinical trial of CRLX101 in combination with chemoradiotherapy in 2015.

In 2011, we initiated an open-label, randomized Phase 2 clinical trial of CRLX101 as monotherapy in patients with advanced non-small cell lung cancer, or NSCLC, who had progressed through one or two prior regimens of chemotherapy. The Phase 2 clinical trial, which enrolled 157 patients, failed to meet its primary endpoint of improvement in overall survival of the CRLX101-treated group as compared to the control arm of best supportive care, which performed substantially better than previously well-established best supportive care benchmarks. However, we observed clear evidence of activity for CRLX101 as measured by RECIST responses and observed progression free survival and overall survival comparable to the progression free survival and overall survival observed in approved cancer therapies in this setting. We believe that this trial of CRLX101 as monotherapy (1) suggests CRLX101 is active in a refractory solid tumor patient population and (2) reinforces CRLX101’s apparently favorable safety profile.

We intend to advance our second product candidate, CRLX301, into a clinical trial by the end of 2014. CRLX301’s anti-cancer payload, docetaxel, is a microtubule stabilizer that is extensively used in clinical practice and is approved by the FDA for the treatment of NSCLC, squamous cell carcinoma of the head and neck, hormone refractory prostate cancer, breast cancer and adenocarcinoma. Based on observations in preclinical tumor models, we believe that CRLX301 has the potential to enhance the clinical efficacy and improve the adverse event profile of docetaxel. We hold issued patents in the United States, Japan and Europe covering the composition of matter of CRLX301 that expire in 2023 and 2024, excluding any potential patent term extension.

In addition to CRLX101 and CRLX301, we have generated additional nanopharmaceuticals using our dynamic tumor targeting platform. We believe that our platform can be used with a wide range of small and large molecule payloads. This provides us with the opportunity to pursue additional product candidate opportunities either by ourselves or in collaborations with pharmaceutical companies using active anti-cancer payloads that would benefit from enhanced tumor targeting, sustained tumor cell drug exposure and reduced systemic drug exposure.

If approved, we expect to commercialize our product candidates in the United States directly with a focused commercialization organization. We expect to seek one or more strategic partners for commercialization of our product candidates outside the United States.

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of nanopharmaceuticals for the treatment of patients with inadequately treated forms of cancer. Key elements of our strategy to achieve this goal are:

- *Advance the clinical development of our lead product candidate, CRLX101, in multiple tumor types.* Based on confirmatory signals observed in the ongoing relapsed renal cell carcinoma clinical trial, we plan to initiate a randomized Phase 2 clinical trial of CRLX101 in combination with Avastin in this indication in the second half of 2014. In 2015, we expect to initiate a randomized Phase 2 clinical trial of CRLX101 in combination with chemoradiotherapy in neoadjuvant rectal cancer and a randomized pivotal clinical trial of CRLX101 in combination with Avastin in relapsed platinum-resistant ovarian cancer, assuming continued confirmatory signals from ongoing CRLX101 clinical trials and adequate additional funding.
- *Advance our second product candidate, CRLX301, into clinical development by the end of 2014.* We intend to initiate a Phase 1 clinical trial of CRLX301 by the end of 2014. Assuming we are successful in establishing a safe maximum tolerated dose in the Phase 1 trial, we plan to advance CRLX301 into Phase 2 development.

- *Leverage our platform to discover and develop a proprietary pipeline of highly differentiated product candidates with small molecule anti-cancer payloads.* Using our dynamic tumor targeting platform, we have created two product candidates, CRLX101 and CRLX301, with small molecule anti-cancer payloads. We have used our platform to create additional nanopharmaceuticals, and we intend over the longer term to develop additional product candidates from the platform.
- *Leverage our platform beyond our proprietary pipeline to enter into strategic partnerships for the development of product candidates.* We believe that our platform can be used with a wide range of small and large molecule payloads, such as RNA. While our focus is on oncology, our preclinical data demonstrates that our platform may also be applicable in certain inflammatory diseases. We plan to explore the possibility of entering into partnerships with companies that have proprietary small or large molecule payloads targeting oncology or inflammation indications. We envision selective partnerships with pharmaceutical companies, in which we would leverage the partner’s expertise, in combination with our platform, to generate novel nanopharmaceuticals incorporating the partner’s approved therapeutic or development candidate.
- *Build core capabilities that allow us to commercialize our products in the United States.* In order to maximize the value of our product candidates, if approved, we expect to commercialize our products in the United States with a focused commercialization organization and to seek one or more strategic partners for commercialization outside the United States.

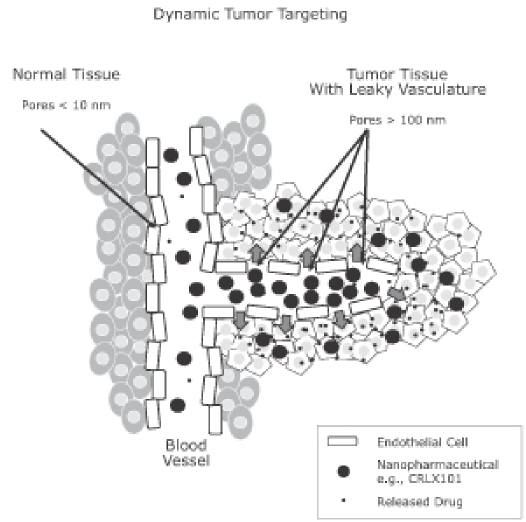
Our Approach to Developing Dynamically Tumor Targeted Nanopharmaceuticals

Our proprietary dynamic tumor targeting platform consists of two technologies: (1) our cyclodextrin polymer containing nanopharmaceutical, or CDP, technology is primarily used for creating nanopharmaceuticals that contain small molecules such as camptothecin in the case of CRLX101 and docetaxel in the case of CRLX301 and (2) our polymeric nanopharmaceutical, or PNP, technology is primarily used for creating nanopharmaceuticals that contain large molecules such as siRNA.

We use both technologies to create nanopharmaceuticals that use a covalent linker to attach an anti-cancer payload to a nanoparticle backbone. The linker determines the release speed of the anti-cancer payload from the nanoparticle backbone. After the anti-cancer payload is released from the nanoparticle backbone, the nanoparticle backbone disassembles into its component polymer strands. The linker and polymer strands in CRLX101 and CRLX301—cyclodextrin, polyethylene glycol, cysteine and glycine—have been extensively used in human pharmaceuticals or are part of humans’ natural metabolism. Our nanopharmaceuticals are too large to be readily eliminated from the bloodstream, but the polymer strands are small enough to be eliminated by the kidneys into the urine. The released anti-cancer payload follows its own metabolic pathway.

Dynamic Tumor Targeting

We believe our dynamic tumor targeting exploits the leaky vasculature present in new blood vessels essential for tumor growth and results in selective uptake of the nanopharmaceutical and sustained release of the nanopharmaceutical’s anti-cancer payload into tumor cells. Based on our preclinical studies and the CRLX101 clinical trials, we believe dynamic tumor targeting involves a three-step process, as described and illustrated below, each of which contributes to the achievement of desirable anti-cancer payload exposure in tumors and the reduction of undesirable anti-cancer payload exposure in normal tissue.



1. *Tumor targeting via leaky vasculature.* After intravenous infusion, the nanopharmaceuticals circulate in the bloodstream. In contrast to typical small molecule drugs, once in the bloodstream, our nanopharmaceuticals are too large to be rapidly eliminated by filtration in the kidneys and to escape from the bloodstream into normal tissue. However, they are small enough to exploit the leaky vasculature found in the immature blood vessels of growing tumors as a selective entry portal into tumor tissue. Generally, pore sizes of normal tissue are less than ten nanometers, and pore sizes of tumor tissue are greater than 100 nanometers. Our CDP-based nanopharmaceuticals are typically between 20 and 40 nanometers in diameter, and our PNP-based nanopharmaceuticals are typically between 60 and 100 nanometers in diameter. As tumors grow, they stimulate the formation of new, immature blood vessels, the inner surfaces of which are less densely lined by endothelial cells as compared to mature blood vessels. As a result, immature blood vessels of growing tumors have larger pores that confer leakiness.

   CRLX101 has a relatively low systemic distribution. A compound’s volume of distribution refers to the fluid volume that would be required to contain the amount of drug present in the body at the same concentration as in the plasma, with higher volume of distribution values indicating more extensive distribution into tissue. In human patients, the volume of distribution of CRLX101 is approximately 2.4 liters. In contrast, in human patients, the volume of distribution of Camptosar® (irinotecan), an analog of camptothecin approved for the treatment of metastatic colon cancer, is approximately 263 liters, and the volume of distribution of Hycamtin (topotecan), an analog of topotecan approved for the treatment of ovarian, cervical and small cell lung cancer, is approximately 130 liters. This low systemic distribution of CRLX101 spares key organ systems from extensive drug exposure. Our nanopharmaceuticals are designed to be stealthy, meaning they are not readily detected by the body’s immune cells and do not readily produce an immune response. This results in slow metabolism and long systemic circulation, allowing our nanopharmaceuticals to penetrate from the bloodstream into tumors via the leaky vasculature.

2. *Transport into tumor cells.* Once inside the tumor, tumor cells actively transport our nanopharmaceuticals into the interior of tumor cells, with macropinocytosis acting as a mechanism of uptake. Macropinocytosis is a cellular uptake mechanism that allows small particles to be transported into cells. It is induced by the tumor’s rapid growth and ensuing demand for cellular building blocks. Macropinocytosis is up-regulated in tumor cells, and CRLX101 exploits this feature to drive active uptake of the nanopharmaceutical and its anti-cancer payload. Following their entry into the cancer cells, we believe our nanopharmaceuticals, due to their size, are not easily removed from cancer cells by efflux pumps. Efflux is the process by which toxic substances are moved out of the cell and which confers tumor resistance against anti-cancer agents.

3. *Sustained release of anti-cancer payload from within tumor cells.* Since the anti-cancer payload is covalently linked to the polymer of the nanopharmaceutical, the anti-cancer payload has to be cleaved from the polymer to be active. We believe the cleavage of the linker connection between the anti-cancer payload and the nanopharmaceutical occurs primarily by hydrolysis and therefore is affected by pH. Typically, the pH level in tumors is lower than in the bloodstream, which further slows the cleavage of the linker and thereby prolongs the release of the anti-cancer payload within tumor cells. We believe sustained release contributes to enhanced anti-tumor activity. In rapidly proliferating cells, such as growing tumor cells, the cell replication cycle takes approximately 24 hours to complete, and the S-phase of the cell replication cycle, during which new DNA is synthesized, lasts for approximately five to eight hours. Many chemotherapeutics, including the camptothecin class, interfere with DNA synthesis during the S-phase, rendering cells more susceptible to inhibition if they are in S-phase and less susceptible to inhibition if they are not in S-phase. Since cells enter the cell replication cycle independently of each other, at any given time not all cells are susceptible to inhibition by an anti-cancer therapy that acts during the S-phase.

   Unless sustained drug concentrations in tumors can be achieved for the entire duration of the replication cycle, the anti-cancer agent will only kill the cells that are in a susceptible phase while drug levels are above the minimum therapeutic threshold, thus allowing the replication and escape of tumor cells during intervals of low drug levels in tumors. For example, topotecan has a terminal half-life, which is the time required for the drug concentration to reach half of its original value, of two to three hours in humans, whereas CRLX101 has a terminal half-life of approximately 28 hours, covering the entire duration of a typical cell replication cycle. Therefore, the third step of dynamic tumor targeting leverages the enrichment of the nanopharmaceuticals within the tumor cells by releasing the payload in a sustained fashion to achieve durable drug concentrations for the entire duration of a typical cell replication cycle.

In each of our preclinical mouse tumor models, our nanopharmaceutical resulted in increased anti-cancer therapeutic benefit compared to the anti-cancer payload alone, which we believe was achieved through targeted delivery and sustained release of a greater amount of anti-cancer payload to tumor cells. In two gastric patients, we had the ability to obtain differential post-therapy biopsies of tumor tissue and adjacent normal tissue. These patient biopsies, taken between 24 and 48 hours after a single dose of CRLX101 was administered, indicated that camptothecin was present in the tumor tissue, and very little camptothecin was present in the adjacent normal tissue. These human data support our belief that our platform achieves higher drug concentrations in tumors compared to normal tissue. In addition, we believe that the safety record observed with our lead drug candidate, CRLX101, across more than 200 cancer patients, can be explained by the targeted delivery of the anti-cancer payload and the sparing of key organ systems from extensive drug exposure.

Application of the Platform

Our platform is applicable to both small and large molecule payloads. It can be applied in oncology, and we believe it may also be applied in certain types of inflammatory diseases where leaky vascular occurs.

We have created nanopharmaceuticals with a variety of small molecule payloads, including camptothecin, docetaxel, Jevtana® (cabazitaxel), Gemzar® (gemcitabine), Trexall® (methotrexate) and Xeljanz® (tofacitinib). We select the small molecule payload based upon several factors, including our ability to conjugate the payload to our polymer, the biological rationale for prolonging circulation and providing sustained release of the payload, and a relatively high potency of the payload. As discussed below, in preclinical testing, our nanopharmaceuticals incorporating small molecule payloads generally show improved pharmacokinetics, activity and tolerability as compared to the payload alone. We intend to develop nanopharmaceuticals alone and potentially in collaboration with partners.

In addition to creating nanopharmaceuticals with small molecule payloads, we have used our platform to create nanopharmaceuticals with large molecule payloads. We have conducted proof of principle experiments to demonstrate that our platform may be able to deliver compounds into tumor cells that are metabolically unstable and would be unable to penetrate tumor cells on their own, such as siRNA, miRNA or mRNA, and that benefit from more selective targeting into tumors, improved uptake into tumor cells and sustained release within tumor cells. Based on these experiments, we believe our platform has the potential to address the delivery challenges, particularly into tumors, of larger and metabolically unstable molecules.

If our platform is able to improve RNA delivery into tumor cells, we believe this would be valuable to companies that are pursuing RNA-based therapeutic approaches in oncology. We do not have the expertise to identify, select, secure and manufacture proprietary anti-cancer RNAs that would be delivered using our platform. Accordingly, we do not intend to focus our business on RNA-based therapeutic approaches, and we would seek to explore this aspect of our platform in collaboration with companies that have expertise in RNA-based therapeutic approaches.

In the future, we may expand beyond anti-cancer therapies to capitalize on the additional opportunities that our platform affords. As an example, in inflammatory diseases our nanopharmaceuticals may offer clinical advantages. Like tumor tissues, in certain inflammatory diseases the pores of blood vessels can become enlarged as part of the inflammatory process. We believe our platform may prove useful in inflammatory diseases characterized by leaky vasculature. While we do not intend to focus our business on inflammatory diseases, this aspect of our platform may afford us with future expansion opportunities by pursuing anti-inflammatory opportunities through collaborations with companies that have expertise in inflammation.

Product Pipeline

Our current development stage pipeline consists of CRLX101 and CRLX301. As described in more detail below, we are pursuing clinical development of CRLX101 in three lead indications, and we intend to begin clinical development of CRLX301 by the end of 2014. The information in the table below is as of March 25, 2014.

Product Candidate	Indication	Stage	Design of Ongoing Clinical Trials and Comments	Planned Trials
CRLX101	Relapsed Renal Cell Carcinoma	Phase 2	• CRLX101 in combination with Avastin • Single-arm, open-label Phase 1b/2 trial that has enrolled 15 of 22 patients • Established Phase 2 dose at 15mg/m^2 for CRLX101 and 10 mg/kg for Avastin • Three of first 11 evaluable patients showed RECIST partial responses	Randomized Phase 2 trial of CRLX101 in combination with Avastin that we intend to commence in second half of 2014

	Relapsed Ovarian Cancer	Phase 2	• Part 1: CRLX101 as monotherapy
			  • Single-arm, open-label Phase 2 trial that is fully enrolled with 29 patients
			  • Met primary efficacy and safety endpoints with two patients still being treated
			• Part 2: CRLX101 in combination with Avastin
			  • Single-arm, open-label Phase 2 trial of CRLX101 in combination with Avastin with two of 43 patients enrolled
			  • Avastin is being provided by Genentech for this study
				Randomized pivotal trial of CRLX101 in combination with Avastin that we expect to commence in 2015

	Neoadjuvant Rectal Cancer	Phase 1b	• CRLX101 in combination with Xeloda and radiotherapy • Single-arm, open-label Phase 1b/2 trial that has enrolled two of 53 patients	Randomized Phase 2 trial of CRLX101 in combination with Xeloda and radiotherapy that we expect to commence in 2015
CRLX301	Solid Tumors	Preclinical	• GLP toxicology studies complete • GMP manufacturing underway	Phase 1/2a trial that we intend to commence by end of 2014

CRLX101

CRLX101 is a dynamically tumor targeted nanopharmaceutical that is administered intravenously. It includes a cyclodextrin containing polymer to which camptothecin is covalently linked. We have demonstrated in preclinical studies that CRLX101 is a potent, durable and combinable inhibitor of topo 1 and HIF. We believe that the properties of CRLX101 could translate into substantial benefits for patients. We are focusing the clinical development of CRLX101 on cancer indications in which we expect the durable inhibition of topo 1 and HIF, in combination with other cancer treatments, to lead to differentiated efficacy. Initially, we are focusing on combinations with VEGF inhibitors or chemoradiotherapy. Accordingly, we are currently developing CRLX101 in combination with Avastin in relapsed renal cell carcinoma and relapsed ovarian cancer and in combination with Xeloda and radiotherapy in neoadjuvant rectal cancer.

Preclinical Efficacy, Potency and Selectivity of CRLX101

Camptothecin is a natural product and a potent inhibitor of topo 1. Camptothecin can exist in two forms: an active lactone form that inhibits topo 1, and an inactive carboxylate form. In human plasma, camptothecin is rapidly converted from its active form to its inactive form. This rapid conversion was not appreciated when camptothecin was originally developed, and in clinical trials patients were dosed until unacceptable toxicities of hemorrhagic cystitis and bone marrow suppression were observed. As a result, camptothecin has never been approved for use by the FDA or any other regulatory agency. To address the issue of rapid conversion of camptothecin to its inactive form, CRLX101 covalently binds camptothecin in its active lactone form to a polymer system that protects camptothecin from metabolism in the plasma, drives delivery of the active form of camptothecin into tumors and tumor cells and minimizes systemic exposure and toxicity related to camptothecin. Within the tumor cells, CRLX101 releases the active form of camptothecin, which can exert its anti-cancer effects.

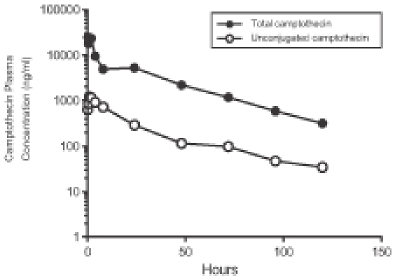
Topo 1 is an essential enzyme required for DNA replication and transcription. In the nucleus, DNA exists as a supercoiled double helix. Topo 1 cuts one DNA strand of the double helix to allow the DNA to uncoil such that the enzyme complexes that drive DNA replication and transcription can access the DNA template. Once these processes are complete, topo 1 re-ligates the DNA back into its super-coiled form. Camptothecin and its analogs, irinotecan and topotecan, bind to the topo 1 DNA complex and prevent the re-ligation of the DNA. The accumulation of unrepaired DNA breaks causes the cell to undergo apoptosis, or cell death. Since tumor cells replicate and transcribe their DNA more frequently than normal cells, they require frequent re-ligation of broken DNA strands and are more sensitive to topo 1 inhibitors than normal cells.

The FDA has approved topotecan for the treatment of ovarian cancer, cervical cancer and small cell lung cancer, and irinotecan for the treatment of metastatic colorectal cancer. Compared to CRLX101, both of these drugs have shorter half-lives, more extensive toxicities and lack of tumor targeting. However, topotecan and irinotecan clinically and commercially validate the inhibition of topo 1 as an important anti-cancer target.

CRLX101 demonstrates a linear and predictable pharmacokinetic, or PK, profile across a number of animal species and in humans. There is little PK variability between doses, between patients and between single and multi-dose administration in patients.

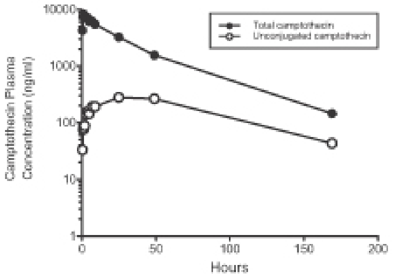
We conducted a preclinical study in which rats were dosed with 2.59 mg/kg of CRLX101, and the concentrations of camptothecin, total and unconjugated, meaning after its release from CRLX101, were measured using liquid chromatography/tandem mass spectrometry. As illustrated in the graph below, plasma concentration of camptothecin in the rats following dosing of CRLX101 declined gradually and lacked a rapid distribution phase. Specifically, the half-life of total camptothecin in the rats in this study was 24 hours following a single dose of CRLX101, whereas the published half-life of camptothecin in rats is only 1.3 hours. Consistent with this prolonged half-life, the clearance of total camptothecin in the study was 1.2 milliliters per hour following a single dose of CRLX101, whereas the published clearance of camptothecin in rats is 1,534 milliliters per hour. The volume of distribution for CRLX101 in rats in the study was 36 milliliters following a single dose of CRLX101, whereas the published volume of distribution of camptothecin in rats is 1,306 milliliters, suggesting less camptothecin is distributed in systemic tissue following a single dose of CRLX101 as compared to camptothecin. The graph below shows the plasma concentration of camptothecin in rats, total and unconjugated, over time following administration of a single dose of CRLX101.

CRLX101 Rat Pharmacokinetic Study



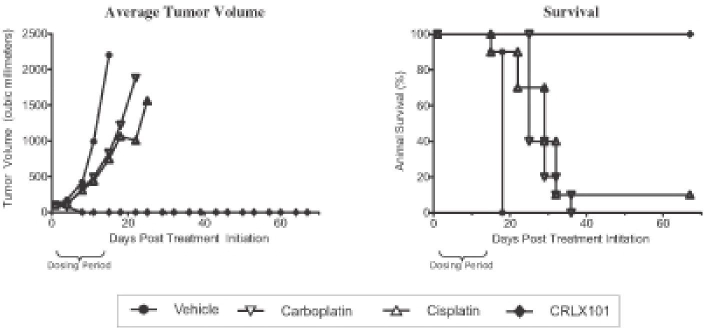
The results from this pharmacokinetic rat study, suggesting long half-life, slow clearance and low volume of distribution, were consistent with the results of our Phase 1/2a clinical trial of CRLX101 in advanced multiply pre-treated solid tumor malignancies, in which human patients were dosed with 15 mg/m^2 of CRLX101. In the Phase 1/2a trial, blood was drawn from patients after their first dose of CRLX101 and analyzed for total and unconjugated camptothecin using liquid chromatography/tandem mass spectrometry. The half-life of CRLX101 following the first dose of CLRX101 in human patients in the trial was 28 hours, the clearance was 91 milliliters per hour and the volume of distribution was 2418 milliliters. The graph below shows the plasma concentration of camptothecin in human patients in the trial, total and unconjugated, over time following administration of a single dose of CRLX101.

CRLX101 Human Pharmacokinetic Data



We have conducted preclinical testing of CRLX101 as monotherapy in over 15 xenograft tumor models, which is a model in which human tumor tissue is transplanted into animals, encompassing colorectal cancer, gastric cancer, head and neck cancer, lymphoma, ovarian cancer, pancreatic cancer, NSCLC, renal cancer, small cell lung cancer and triple negative breast cancer. In our xenograft tumor model studies, CRLX101 demonstrated superiority over commercial comparator drugs as measured by median survival, tumor shrinkage and tumor growth delay. In these tumor model studies, the commercial drugs were administered at their respective optimal doses and dosing schedules, as determined by the literature. In several of these tumor model studies, CRLX101 achieved complete tumor eradication, which was not achieved by the commercial drugs tested in these models.

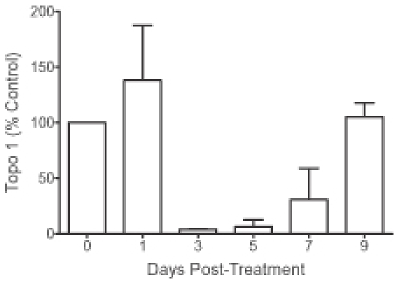
The following graphs illustrate the tumor volume results and post-treatment survival rates in a preclinical study comparing CRLX101 to Paraplatin® (carboplatin) and cisplatin, which are platinum-based chemotherapeutic agents, in an ovarian xenograft model. In this study, we treated nude mouse xenograft models in which human A2780 ovarian cancer tumor cells were implanted subcutaneously in mice and allowed to establish tumors. We administered 10 mg/kg of CRLX101, 7 mg/kg of cisplatin, 100 mg/kg of carboplatin or saline, which we also refer to as the vehicle, by intravenous infusion. Each dose group consisted of ten animals and all mice were treated weekly for three weeks. All dose levels were close to the maximum tolerated dose in this model. CRLX101, carboplatin and cisplatin all delayed tumor growth and improved survival rates as compared to the saline-treated mice, however, as compared to both carboplatin and cisplatin, the CRLX101-treated mice displayed much higher tumor regression, and 100% tumor-free survivors at the conclusion of the study. These results are illustrated in the graphs below.



Our preclinical testing of CRLX101 in combination therapy in multiple xenograft models and one orthotopic model, which is a model in which a tumor is grafted into the animal in its natural location, encompassing renal cell carcinoma, ovarian cancer, head and neck cancer, and triple negative breast cancer, demonstrated additive or synergistic effect when CRLX101 was combined with chemotherapy, platinum, VEGF inhibitors or radiotherapy.

We conducted a preclinical study in which a single 6 mg dose of CRLX101 reduced available topo 1 protein for at least one week. We treated 18 nude mouse xenograft models (three per time point) in which human NCI-H1299 non-small cell lung cancer tumor cells were implanted subcutaneously in mice and allowed to establish tumors. We administered a single dose of 6 mg/kg CRLX101 or saline (vehicle) to the control group and collected tumors at various time points, including one, three, five, seven and nine days after treatment using western blot analysis. Tumors were flash-frozen and topo 1 protein levels were measured and calculated as a percentage of topo 1 protein levels in saline-treated mice. As shown in the graph below, a single 6 mg/kg dose of CRLX101 reduced available topo 1 protein, and topo 1 protein recovered to baseline levels by nine days after treatment.

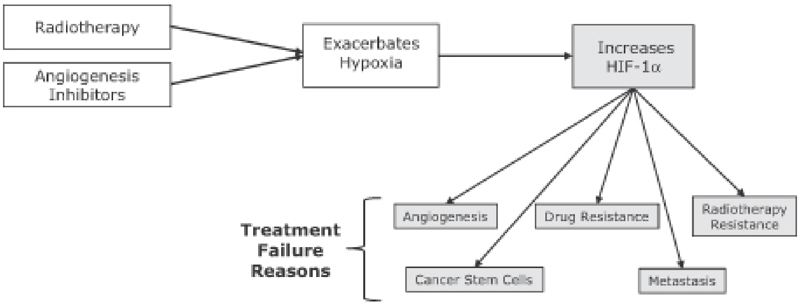
Topo 1 Protein in Tumors After CRXL101 Treatment



In addition to inhibiting topo 1, CRLX101 is a potent, durable and combinable inhibitor of HIF-1a and HIF-2a protein expression. The compounds in the camptothecin compound family, including camptothecin and topotecan, have been described as inhibitors of HIF-1a in the past. However, the literature suggests that to achieve durable inhibition of HIF-1a, sustained concentrations of camptothecin must be achieved within tumor cells. Due to its short half-life, low tumor targeting and high toxicities, topotecan cannot effectively achieve durable HIF-1a inhibition.

HIF-1a has recently become a target of increasing interest in cancer research. The literature on the subject has grown substantially and, as summarized in a review paper published in *Nature Reviews Clinical Oncology* in 2012, many believe that HIF-1a is a master regulator for many cancer cell survival pathways. When cancer cells proliferate, they can become starved of oxygen, or hypoxic, as tumor growth outpaces the growth of new blood vessels. The lack of oxygen can be exacerbated when new blood vessel formation is inhibited by anti-angiogenesis drugs, such as Avastin, Zaltrap and Votrient, or as a consequence of radiotherapy. Under hypoxic conditions, the normal degradation of HIF-1a slows down, thus leading to a buildup of HIF-1a. According to the *Nature Reviews Clinical Oncology* paper, independent researchers have demonstrated that the buildup of HIF-1a in turn up-regulates cancer cell survival pathways such as angiogenesis, drug resistance, radiotherapy resistance, cancer stem cell formation and metastasis. Cancer stem cells are associated with therapy resistance and cancer metastasis. While anti-angiogenesis drugs can achieve impressive tumor shrinkage and progression free survival benefits in patients, they often fail to improve overall survival. This lack of consistent correlation of tumor response to survival following treatment with anti-angiogenesis drugs may be ascribed to hypoxia-induced up-regulation of HIF-1a and the consequent triggering of cancer cell survival pathways that permit a sub-population of cells to survive treatment and regrow the tumor in a more aggressive form.

The graphic below illustrates the role of HIF-1a in up-regulating cancer cell survival pathways in hypoxic conditions in tumor cells, which are exacerbated by radiotherapy and angiogenesis inhibitors, such as Avastin, Zaltrap and Votrient.



HIF-a may be a major factor in explaining why oxygen-deprived tumors can survive and trigger the formation of heterogeneous, resistant and distant tumors. Therefore, HIF-1a has emerged as an important target for cancer research. To effectively inhibit HIF-1a, however, we believe durable target inhibition is required. Topotecan and irinotecan have been shown to inhibit HIF-1a only transiently and metronomic dosing of topotecan and irinotecan is believed to provide a more durable inhibition of HIF-1a, but these dosing regimens have not been shown to be clinically feasible due to excessive toxicity encountered at the approved doses of these drugs. To our knowledge, there is no other durable and tumor targeted inhibitor of HIF-1a currently on the market or in advanced clinical development, thus making CRLX101 unique in this respect. We expect that the simultaneous inhibition of topo 1 and HIF-1a by CRLX101 could lead to a significant clinical benefit, particularly if combined with anti-cancer therapies that are known to create hypoxia and up-regulate HIF-1a.

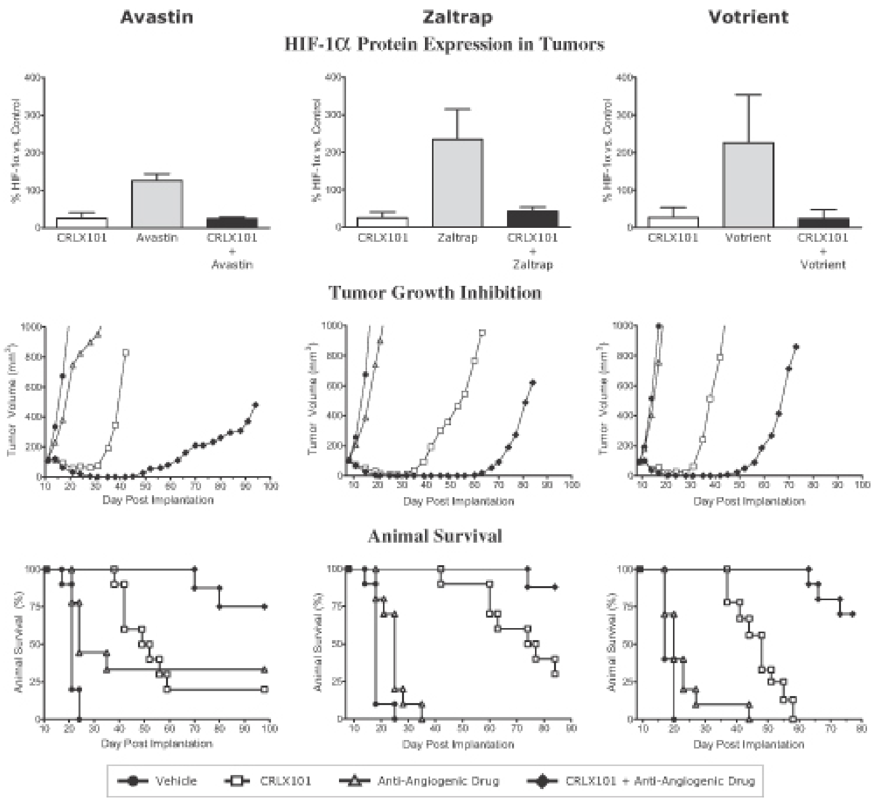
Not only have we shown that CRLX101 inhibits HIF-1a in preclinical tumor models, but we have also demonstrated that it is synergistic with Avastin in an ovarian xenograft model. We believe that this synergy is at least partly caused by the ability of CRLX101 to inhibit the up-regulation of HIF-1a caused by anti-angiogenic therapy. We have further confirmed this synergy in a highly metastatic ovarian cancer orthotopic tumor model, as well as in a triple-negative breast cancer orthotopic tumor model. We have also observed the synergy of CRLX101 with other VEGF inhibitors such as Votrient and Zaltrap.

We have conducted animal tumor model studies comparing CRLX101 to certain leading anti-angiogenesis drugs and the combination of CRLX101 and these anti-angiogenesis drugs. In these studies, we treated nude mouse xenograft models in which human A2780 ovarian cancer tumor cells were implanted subcutaneously in mice and allowed to establish tumors. We administered 5 mg/kg CRLX101 weekly by intravenous infusion alone or in combination with one of three different antiangiogenic drugs: Avastin, Zaltrap or Votrient. Avastin was dosed intravenously at 5 mg/kg twice per week. Zaltrap was dosed intraperitoneally at 25 mg/kg twice per week. Votrient was dosed orally at 150 mg/kg daily. Vehicle-treated mice were dosed with saline. Each dose group consisted of ten animals. We administered a CRLX101 dose level that was half the maximum-tolerated dose so that we could compare the effect of the applicable CRLX101 combination to CRLX101 as monotherapy. All other dose levels were the maximum effective dose in this model, as indicated by the literature. For the analysis of HIF-1a in tumors, mice were dosed for ten days, and three days following the final dose tumors were flash-frozen and HIF-1a protein levels were measured via western blot analysis, quantified using infrared fluorescence detection, normalized to actin levels and compared to HIF-1a protein levels from saline-treated mice. For the survival analysis, mice were dosed for three weeks, tumors were measured using calipers twice per week, and each animal was euthanized at the earlier of the time when its tumor reached a volume of 2,000 cubic millimeters or the end of the study.

In these animal tumor model studies:

- HIF-1a protein expression was significantly up-regulated in the presence of each tested anti-angiogenesis drug;
- HIF-1a protein expression was significantly down-regulated when exposed to a low dose of CRLX101;
- when CRLX101 was combined with any of the tested anti-angiogenesis drugs, HIF-1a protein expression was down-regulated compared to control, thus confirming that the CRLX101 down-regulation can counteract the HIF-1a protein expression up-regulation normally produced by these anti-angiogenesis drugs alone; and
- the combination of a low dose of CRLX101 with the anti-angiogenesis drugs was synergistic and resulted in markedly longer animal survival than either drug by itself.

These HIF-1a protein expression and survival rate results are illustrated in the graphs below.



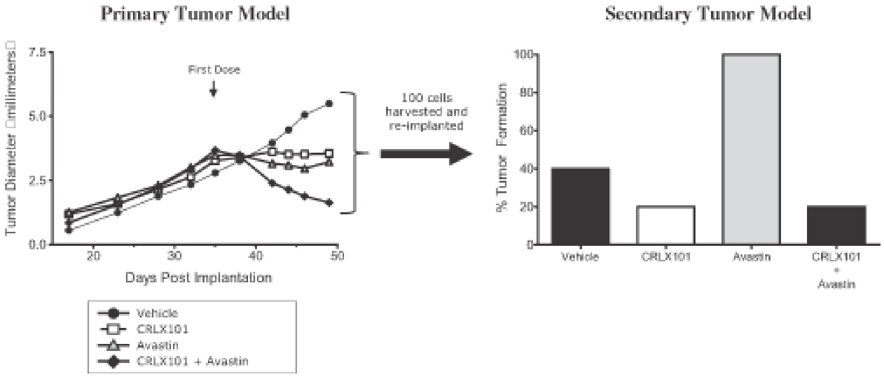
We have achieved similar results in a preclinical study of the effect on cancer stem cells of exposure to CRLX101 alone and CRLX101 in combination with Avastin. In this study, we treated nude mouse xenograft models in which human SUM159 triple-negative breast cancer tumor cells were implanted orthotopically in mice and allowed to establish tumors. We administered 6 mg/kg of CRLX101 weekly by intravenous infusion alone or in combination with Avastin. Avastin was dosed intravenously at 5 mg/kg twice per week. Each dose group consisted of 20 or more mice. We administered a CRLX101 dose level that was half the maximum-tolerated dose so that we could compare the effect of the CRLX101-Avastin combination to CRLX101 as monotherapy. The

Avastin dose level was close to the maximum effective dose in this model, as indicated by the literature. Vehicle-treated mice were dosed with saline. Mice in the primary tumor group were dosed for two weeks and tumor volume was measured. As can be observed in the primary tumor growth plot below, CRLX101 as monotherapy and Avastin as monotherapy each resulted in some tumor growth inhibition, and the combination of CRLX101 and Avastin resulted in increased tumor growth inhibition. At the end of these two weeks, tumors were extracted and 100 tumor cells were implanted orthotopically into new, untreated mice. This secondary group of mice was observed for 90 days without treatment, and the percentage of these mice that grew new tumors is plotted in the graph below as the percentage of tumor formation. Tumors that are enriched for cancer stem cells in the primary tumor model are more likely to grow new tumors in the secondary tumor model, that is, tumors enriched for cancer stem cells have a greater tumor-initiating capacity, and tumors that have lower numbers of cancer stem cells in the primary tumor model will have a lower tumor-initiating capacity.

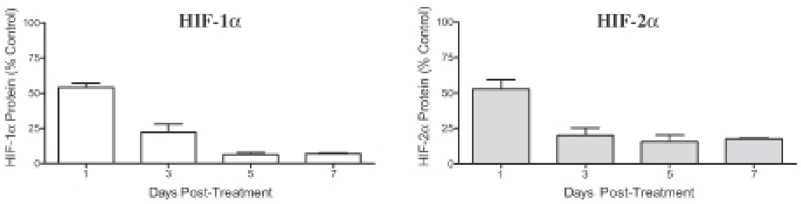
In these cancer stem cell functional experiments:

- pre-treatment with CRLX101 led to a reduction in tumor-initiating capacity, consistent with a reduction in the number of cancer stem cells in the primary tumors;
- pre-treatment with Avastin led to greater tumor-initiating capacity compared to control, consistent with an increase in the number of cancer stem cells in the primary tumors; and
- pre-treatment with a combination of CRLX101 and Avastin led to a reduction in the tumor-initiating capacity compared to Avastin treatment alone, thus demonstrating that CRLX101 may reduce the number of cancer stem cells in primary tumors induced by Avastin pre-treatment.

The primary and secondary tumor model results from these cancer stem cell functional experiments are illustrated in the graphs below.



In addition to inhibiting HIF-1a, CRLX101 also appears to durably inhibit HIF-2a. In a preclinical study, we treated nude mouse xenograft models in which human HCT-116 colorectal cancer tumor cells were implanted subcutaneously in mice and allowed to establish tumors. We administered a single dose of 6 mg/kg CRLX101 or saline (vehicle) to the control group and collected tumors at four different time points: one, three, five and seven days after treatment using western blot analysis. Tumors were flash-frozen and HIF-1a and HIF-2a protein levels were measured via western blot analysis, quantified using infrared fluorescence detection, normalized to actin levels and calculated as a percentage of HIF protein levels in saline-treated mice. As shown in the graph below, in each case, a single 6 mg/kg dose of CRLX101 reduced HIF-1a by over 90%, and reduced HIF-2a by approximately 80% in tumor tissue, in each case compared to control beginning three days after treatment and continuing for as long as one week.


HIF Protein Expression in Tumors After CRLX101 Treatment

Radiotherapy is frequently used for the treatment of solid tumor malignancies that have not extensively metastasized and are accessible, and thus a radiation beam can be deployed with the goal of destroying the tumor. For example, rectal cancer and head and neck cancers are often treated with radiotherapy. Radiotherapy causes single strand DNA breaks in the irradiated tumor cells and, if not repaired, these DNA single strand breaks lead to the death of the irradiated tumor cells. However, the enzyme topo 1 has the ability to re-ligate DNA single strand breaks and repair the radiotherapy-caused DNA damage, thereby saving the tumor cells from cell death and reducing the efficacy of radiotherapy. As a result, there is interest in combining radiotherapy with topo 1 inhibitors to enhance the effects of radiotherapy, i.e. as a radiosensitizer. However, the combined toxicities of radiotherapy and either irinotecan or topotecan, the two approved topo 1 inhibitors, are often too severe for this therapy to be clinically useful.

Radiotherapy also causes extensive cell damage, which leads to hypoxic regions in the irradiated tumors. This hypoxia results in the up-regulation of HIF-1a, which in turn has been shown to up-regulate cancer cell survival pathways and thereby reduce the effectiveness of radiotherapy. Thus, a beneficial chemotherapeutic agent to combine with radiotherapy would be (1) a topo 1 inhibitor to prevent the repair of radiotherapy-induced single-strand DNA breaks as a radiosensitizer, (2) a HIF-1a inhibitor to prevent the radiotherapy-induced up-regulation of HIF-1a and its associated induced resistance to radiotherapy, (3) an agent with a favorable safety profile to allow the combination with radiotherapy and (4) an agent with durable topo 1 and HIF-1a inhibition since radiotherapy is frequently administered daily and thus requires durable counteracting of DNA repair and HIF-1a up-regulation. We believe that CRLX101 may be a beneficial agent for combination with radiotherapy since it satisfies all of the above criteria. This is evidenced by an animal tumor model of head and neck cancer in which CRLX101 was shown to be a potent radiosensitizer, thus suggesting that CRLX101 may have clinical utility in combination with radiotherapy in certain cancer types.

CRLX101 Clinical Development

Based on the properties of CRLX101, we have prioritized its clinical development in accordance with the following criteria:

- Topo 1-sensitive tumor types
- HIF-driven tumor types
- Solid tumors with increased hypoxia as a result of radiotherapy or anti-angiogenic drugs
- Potential for synergy in combination with radiotherapy or VEGF inhibitors
- Earlier lines of therapy with less advanced tumors in which the durable inhibition of HIF may confer greater benefit in preventing therapy resistance and metastases

Accordingly, we currently are focusing on combinations with other cancer therapies in three indications: relapsed renal cell carcinoma in combination with Avastin, relapsed ovarian cancer in combination with Avastin and neoadjuvant rectal cancer in combination with Xeloda and radiotherapy.

CRLX101 Phase 1/2a Clinical Trial

In 2011, we completed a Phase 1/2a clinical trial of CRLX101 in 62 patients with advanced multiply pre-treated solid tumor malignancies. This clinical trial began in June 2006. From June 2006 to June 2009, Calando Pharmaceuticals, Inc., or Calando, conducted a Phase 1 trial of CRLX101, in which it dosed 18 patients. We continued the Phase 1 trial from June 2009 to April 2010 and then began the Phase 2a portion of the trial. Ultimately, the Phase 1 portion of the trial enrolled a total of 24 patients, and from April 2010 to January 2011, we enrolled 38 patients in the Phase 2a portion.

Results from the Phase 1 portion of the clinical trial showed that patients were able to tolerate CRLX101 administered intravenously at a maximum tolerated dose of 15mg/m^2 camptothecin equivalent every two weeks and that toxicities at this dose were generally low grade and reversible upon termination of treatment. The primary dose limiting toxicity identified in the Phase 1 portion of the clinical trial was neutropenia, which is a well-documented side effect of many chemotherapeutic agents and is considered an on-target effect resulting from the activity of topo 1 inhibitors, such as camptothecin, in the bone marrow.

After determination of the maximum tolerated dose in the Phase 1 portion of the clinical trial, an additional 38 patients were enrolled in a Phase 2a maximum tolerated dose expansion cohort, with a focused selection of patients with cancer types that historically have demonstrated sensitivity to topo 1 inhibitors, including 21 NSCLC patients. Pursuant to the design of the trial, CRLX101 treatment continued until disease progression, which was determined based on RECIST criteria, patient withdrawal, excessive toxicity or adverse events delaying treatment for 28 days or resulting in death. Patients continuing CRLX101 treatment also received additional supportive care. A total of 44 patients, six of whom were in the Phase 1 portion and 38 of whom were in the Phase 2a portion of the trial, with an average of 3.5 prior regimens of therapy, received CRLX101 at the maximum tolerated dose of 15mg/m^2. Mean elimination unconjugated T_{max} values, which is the time after administration of a drug when the maximum plasma concentration is reached, generally ranged from 17.7 to 24.5 hours, confirming the sustained release of camptothecin. Maximum plasma concentrations and areas under the curve were generally proportional to dose for both conjugated and unconjugated camptothecin confirming consistent camptothecin release at different dose levels. The primary objectives of the Phase 1/2a clinical trial were to determine the safety, toxicity, maximum tolerated dose and plasma PK of CRLX101 when administered intravenously to patients with advanced solid tumor malignancies. All of the objectives of the Phase 1/2a trial were met.

RECIST defines disease progression and tumor response based on the sum of the longest diameters of a set of target tumor lesions identified when the patient enters the trial, which we refer to as baseline. A 20% or greater increase in the sum of diameters in target lesions as compared to baseline, or unequivocal progression in non-target lesions, or the appearance of a new lesion, is defined as progressive disease. A reduction in the sum of the diameters of at least 30% as compared to baseline and no new lesions is defined as a partial response. A complete disappearance of target and non-target lesions, and the normalization of any tumor markers, constitutes a complete response. Both partial and complete responses must be confirmed by repeat assessments at least four weeks after the partial or complete response is first documented. Stable disease refers to patients who exhibit neither response nor disease progression. Objective response rate is typically defined as the sum of the patients with partial and complete response divided by the number of patients.

Median progression free survival for patients treated in the Phase 1/2a trial at the maximum tolerated dose was 3.7 months. The best response per RECIST criteria was stable disease in 28 patients, or 64%, treated at the maximum tolerated dose, of which 15 patients, or 34%, had confirmed stable disease at subsequent evaluations. Six patients went on to receive treatment with CRLX101 for longer than six months, and one such patient with pancreatic cancer with liver and lung metastases experienced stable disease and received a total of 24 cycles of CRLX101 at 6 mg/m^2 weekly dosing prior to discontinuing for progressive disease, or PD. In a subset of 22 patients with NSCLC, median progression free survival was 4.4 months for all patients and 4.8 months for patients with non-squamous histology, and stable disease was reported in 16 patients, or 73%, eight of whom had confirmed stable disease at subsequent evaluations. None of the patients treated in the Phase 1/2a trial reported excessive treatment-related toxicities or treatment-related adverse events resulting in death.

CRLX101 Phase 2 Clinical Trial in NSCLC

In 2011, we began 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, which we also refer to as second and third line therapy, respectively, of chemotherapy. This clinical trial was conducted under an investigational new drug application, or IND, and we enrolled 157 patients between July 2011 and April 2012 at sites in Russia and the Ukraine. The trial had a treatment arm, which consisted of patients treated with CRLX101 and best supportive care, and a comparator arm, which consisted of patients receiving best supportive care. For every two patients enrolled in the CRLX101 treatment arm, one patient was enrolled in the best supportive care comparator arm.

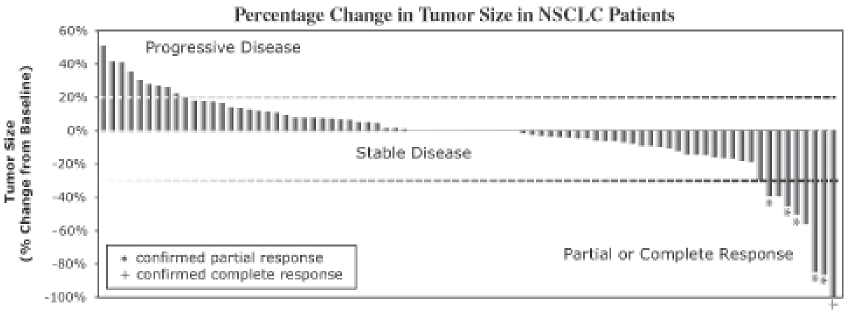
This Phase 2 clinical trial failed to meet its primary endpoint, which was improvement in overall survival of the CRLX101 intention to treat group as compared to the best supportive care arm of the trial. The difference in the overall survival of the CRLX101 intention to treat group as compared to the best supportive care arm of the trial was analyzed with a log rank test in a Kaplan-Meier survival model. The p-value associated with this test was not statistically significant ($p=0.14$). In clinical trials comparing CRLX101 to a control using a specified endpoint, the p-value is a measure of compatibility between the observed outcomes and the hypothesis that there is no treatment effect attributable to CRLX101; the p-value represents the likelihood that the observed outcome occurred by chance alone. Adverse events experienced in the CRLX101 arm of the trial were generally low grade and manageable and were similar to the adverse events experienced on the best supportive care arm of the trial. This adverse event profile was consistent with the adverse events seen in other clinical trials of CRLX101. Secondary endpoints of the trial included safety, tolerability, median progression free survival time, objective response rate and overall survival in particular patient subgroups. Although the trial failed to meet its primary endpoint, we observed evidence of activity for CRLX101 as measured by RECIST responses and observed progression free survival and overall survival comparable to the progression free survival and overall survival observed in approved cancer therapies in this setting. Disease progression and tumor response rates were determined in accordance with RECIST criteria.

Median overall survival for patients administered CRLX101 was 6.3 months compared to 11.9 months for patients administered best supportive care. However, the best supportive care population was significantly enriched for more slowly progressing patients primarily because of (1) selective patient withdrawal, which was possible due to the open-label protocol of the trial, and (2) access to post-treatment therapy; we did not anticipate either of these factors when the trial protocol was developed. An analysis of the patient populations indicated that 16% of the best supportive care patients, versus 5% of the CRLX101 treated patients, withdrew from the trial before or during the first treatment cycle, which was four weeks in duration. The patients who withdrew from the best supportive care arm were more rapidly progressing than the remaining patients in the best supportive care arm, as measured by prognostic factors including a high percentage of males, a shorter time since initial diagnosis and a shorter time since relapse. The result was that rapid progressors tended to withdraw from the best supportive care arm while slower progressors tended to remain in the best supportive care arm. A time to treatment failure analysis confirmed the impact of the selective withdrawal of the best supportive care patients since the median time to treatment failure for best supportive care patients was 1.7 months, compared to 2.1 months for the CRLX101 patients. In addition, 40% of the best supportive care patients received post-trial cancer therapy, versus 28% of the CRLX101 treated patients.

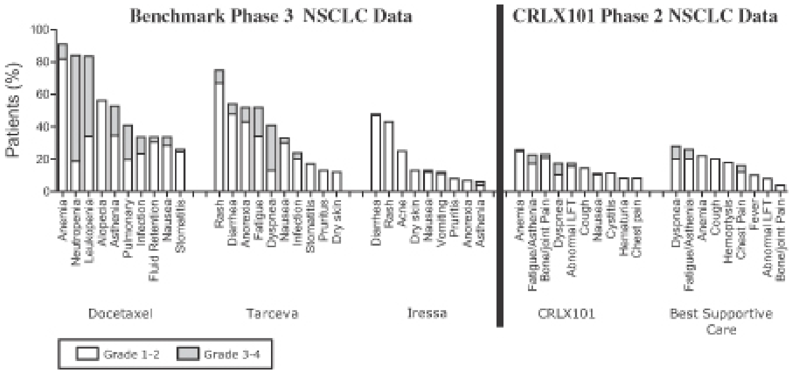
We believe these imbalances in withdrawal rates and post-trial cancer treatment between the CRLX101 and best supportive care arms caused an upward skewing of the median overall survival of the best supportive care population. This belief is supported by benchmark data on median overall survival in previous second and third line registration trials of Iressa® (gefitinib), Tarceva® (erlotinib) and docetaxel in NSCLC. For example, the 11.9 month median overall survival of the best supportive care population observed in our trial (1) is more than double the median overall survival for the relevant second and third line best supportive care benchmarks in NSCLC, which range from 4.6 to 5.1 months; and (2) greatly exceeds the median overall survival for second and third line approved treatments for NSCLC, which range from 5.6 to 7.5 months.

Even if the best supportive care arm of the trial had performed in line with Phase 3 benchmarks, we believe the NSCLC trial would have failed to meet its endpoint because the results of the CRLX101 treatment arm did not meet our expectations. As a result, we are not planning further clinical development in this indication, however, based on several analyses, we believe that this trial of CRLX101 as monotherapy provides important information for the CRLX101 development program (1) suggesting CRLX101 is active in a refractory solid tumor patient population and (2) reinforcing CRX101’s apparently favorable safety profile.

The following graph shows the change in tumor size for the 81 NSCLC patients who received CT scans on the CRLX101 arm of the NSCLC trial. Each vertical bar in the graph represents the percentage change in tumor size from the time when the patient entered the clinical trial until the largest tumor size reduction or smallest tumor size growth, as applicable, was measured for that patient in accordance with RECIST. These results reflect that the majority of patients treated with CRLX101 in the trial achieved disease control, which includes stable disease, partial responses and complete responses. Six of the eight RECIST responses were confirmed by a subsequent CT scan, one of which was a complete response.

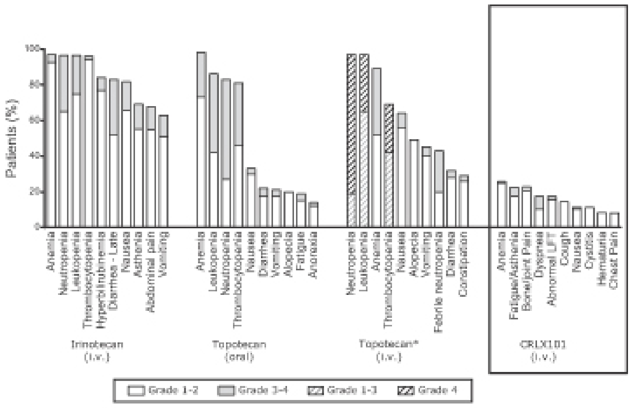


The adverse events experienced in the CRLX101 arm of the clinical trial were generally low grade and manageable. They were similar to the adverse events experienced on the best supportive care arm of the trial, and they were relatively less severe than the adverse events experienced in clinical trials of docexatel, Tarceva and Iressa, as illustrated by the graphs below.



Potential for Combinability

A comparison of the adverse events experienced by patients in the CRLX101 arm of the NSCLC clinical trial to the adverse events experienced by patients in clinical trials of approved camptothecin-class therapeutics, irinotecan and topotecan, further confirms the apparently favorable safety profile of CRLX101. As illustrated in the graphs below, the adverse events experienced by patients in the CRLX101 arm of the NSCLC trial were generally less severe than those experienced by patients in the clinical trials of irinotecan and topotecan. We believe that CLRX101's apparently favorable safety profile supports our view that CRLX101 may be combinable with anti-cancer therapies.



* The label for i.v. topotecan categorizes non-hematological adverse events as (a) Grade 1-2 and (b) Grade 3-4, but it categorizes hematological adverse events as (a) Grade 1-3 and (b) Grade 4, so these adverse events are shown with diagonal stripes.

Ongoing CRLX101 Clinical Trials

Relapsed Renal Cell Carcinoma

Current Treatments for Renal Cell Carcinoma: The American Cancer Society estimated that 65,000 new cases of kidney cancer would occur in the United States in 2013 and that approximately 14,000 people would die from kidney cancer in 2013. According to the Surveillance, Epidemiology, and End Results (SEER) Program of the United States National Cancer Institute, the incidence of kidney cancer appears to be rising. Renal cell carcinoma is by far the most common type of kidney cancer; approximately nine out of ten kidney cancers are renal cell carcinomas. There is currently no cure for renal cell carcinoma that has metastasized beyond the lymph nodes to one or more distant organs, which we refer to as metastatic renal cell carcinoma. The majority of patients with metastatic renal cell carcinoma progress to a third line treatment regimen, and there is currently no treatment specifically approved for use in third line treatment of renal cell carcinoma. This unmet need creates an opportunity for a new class of therapies in this indication.

Systemic therapeutic options for advanced stage renal cell carcinoma include molecularly targeted therapies and, less often, chemotherapy and immunomodulatory therapies such as interferon alpha and interleukin-2. Molecularly targeted therapies used for the treatment of renal cell carcinoma have only modestly extended the median overall survival of patients.

While there are currently six FDA-approved therapies commonly used for the treatment of renal cell carcinoma, they represent only two mechanistic classes—those that target VEGF signaling, including tyrosine kinase inhibitors, or TKIs, and those that inhibit the mammalian target of rapamycin, or mTORIs. Recent drug development has focused on improvements within these classes but has produced only incremental gains such as the two-month progression free survival advantage of Inlyta® (axitinib) over Nexavar® (sorafenib) in the second-line treatment of advanced renal cell carcinoma. No new class of targeted therapy has been introduced in the field since the mTORI, Torisel® (temsirolimus), in 2007. A second mTORI, Afinitor® (everolimus), was shown to extend progression free survival only modestly over placebo in the second-line setting, from 1.9 months to 4.9 months. We believe that there is a significant need for therapeutics with novel properties, such as CRLX101, to treat relapsed renal cell carcinoma.

Rationale for Use of CRLX101 for Relapsed Renal Cell Carcinoma: Clear cell renal cell carcinoma comprises approximately 85% of renal cell carcinomas. The most commonly identified genetic aberrations in clear cell tumors are mutations of the von Hippel Lindau tumor suppressor gene and the reduction or loss of its tumor suppressor function. This loss in turn leads to higher intracellular levels of HIF-1a and HIF-2a, resulting in paracrine signaling, which is a form of cell-to-cell communication in which a cell produces a signal that alters the behavior or differentiation of nearby cells, by tissue growth factors such as VEGF, a key mediator of angiogenesis. Therefore, angiogenesis is an early pathophysiologic step in the tumorigenesis and disease progression in many renal cell carcinomas.

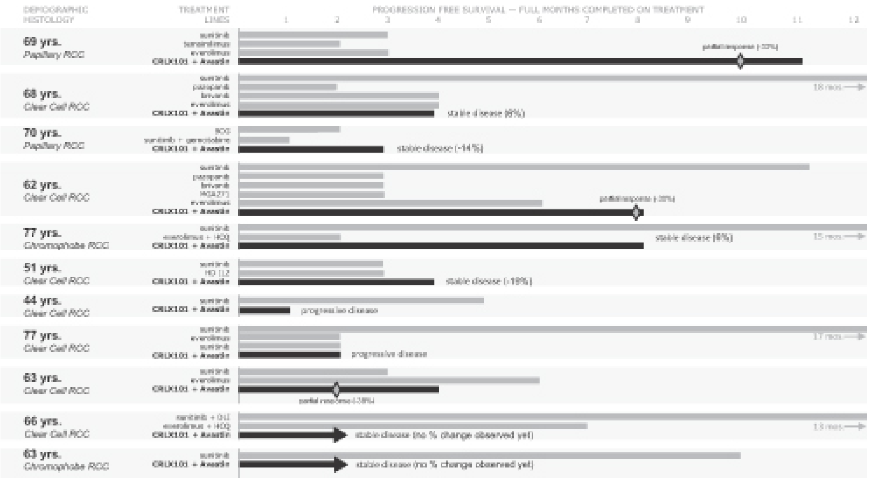
As highlighted above, CRLX101 appears to durably suppress HIF-1a and HIF-2a in preclinical animal studies and has demonstrated notable synergy in combination with VEGF inhibitors including Avastin. We hypothesize that a CRLX101-mediated override of acquired resistance to Avastin, achieved through the inhibition of HIF, could facilitate the translation of progression free survival and response rate benefits achieved with Avastin in this setting into meaningful overall survival benefits for renal cell carcinoma patients.

Our preclinical data suggest that CRLX101 is an inhibitor of both HIF-1a and HIF-2a protein expression. While the role of HIF-1a as a master regulator of cancer cell survival pathways is well documented, the exact role of HIF-2a is generally less well described. Both HIF-1a and HIF-2a expression have been shown to correlate with poor prognosis in multiple tumor types. But in the case of renal cell carcinoma, the specific roles of HIF-1a and HIF-2a are not yet well understood. Some leading oncologists and researchers have suggested that inhibiting HIF-1a and HIF-2a simultaneously may be better than inhibiting HIF-1a or HIF-2a individually.

We have chosen Avastin as a CRLX101 combination therapeutic for several reasons. Avastin is a monoclonal antibody with affinity for VEGF that demonstrates clinically worthwhile activity in the treatment of advanced renal cell carcinoma and is approved by the FDA for use in the treatment of patients with metastatic renal cell carcinoma. Additionally, Avastin is generally well tolerated and its adverse event profile does not appear to overlap to a large extent with the adverse event profile of CRLX101. Avastin has a track record of success in enhancing the activity of chemotherapy in the treatment of solid tumors, and it is an active compound. By contrast, the less selective orally available small molecule inhibitors have been difficult to combine with chemotherapy and have shown mixed clinical activity usually accompanied by enhanced toxicity. In addition, Avastin has been successfully combined with multiple chemotherapeutic agents, including the topo 1 inhibitor irinotecan. Finally, Avastin is administered by intravenous infusion once every two weeks, as is CRLX101, facilitating the administration of CRLX101 and Avastin as combination therapy.

Clinical Development of CRLX101 in Relapsed Renal Cell Carcinoma: A Phase 1b/2 open-label IST evaluating CRLX101 in combination with Avastin is enrolling patients at the University of Pennsylvania, and the trial is expected to expand to Thomas Jefferson University. Relapsed renal cell carcinoma patients with metastatic or locally advanced disease who have been treated with at least one prior molecularly targeted therapy are eligible to participate in the trial. Two dose-levels of CRLX101, 12 mg/m^2 and 15 mg/m^2, delivered intravenously once every two weeks, are being evaluated in combination with standard Avastin dosing of 10 mg/kg delivered intravenously once every two weeks. This clinical trial employs a two-stage design, with 12 patients to be treated in an initial dose finding stage and an additional ten patients to be treated at the maximum tolerated dose of CRLX101 administered in combination with Avastin. CT-based tumor evaluations are planned to occur every two cycles. The primary endpoint of the Phase 1b stage was to identify the maximum tolerated dose of CRLX101 in combination with Avastin in this indication, and the primary endpoint of the Phase 2 stage is progression free survival at four months in 11 or more of the 22 patients on the trial. Secondary objectives include objective response rate and assessment of toxicity. As of March 25, 2014, 15 patients have been enrolled in this clinical trial, enrollment is ongoing and the CRLX101-Avastin combination appears well tolerated with no drug-related serious adverse events reported.

The graph below shows, for each of the 11 patients in this trial who have been treated with the CRLX101-Avastin combination and are evaluable as of March 25, 2014, prior treatment lines, percentage change in tumor size, RECIST response and progression free survival. The percentage change in tumor size represents the percentage change from the time when the patient entered the clinical trial until the largest tumor size reduction or smallest tumor size growth, as applicable, as measured for that patient in accordance with RECIST. The changes in tumor size are unaudited and based on CT-scan assessment performed at the treatment center.



Of the 11 patients evaluable in this trial as of March 25, 2014, three patients, or 27%, have demonstrated confirmed RECIST partial responses. The RECIST partial response rate of three of the 11 evaluable patients is encouraging because several recent studies in advanced renal cell carcinoma suggest that after treatment with a TKI such as Sutent® (sunitinib), subsequent therapies, including Avastin alone, achieve RECIST partial response rates of only between 2% and 4%. While there are a small number of patients in the trial, and only 11 have been evaluated as of March 25, 2014, a partial response rate that appears to be substantially higher than the response rate reported in the literature for a TKI pre-treated renal cell carcinoma patient population suggests that the preclinical synergy between CRLX101 and Avastin may translate into differentiated therapeutic benefit in advanced renal cell carcinoma.

Based on results observed to date in the Phase 1b/2 trial and discussions with key investigators in the field, we intend to evaluate the CRLX101-Avastin combination in a randomized, well-controlled Phase 2 clinical trial beginning in the second half of 2014. We plan to conduct this CRLX101-Avastin combination trial in third line relapsed renal cell carcinoma patients having progressed through both prior VEGF inhibiting therapy and prior mTORI therapy with a comparison made to the standard of care in this setting. We expect to design the trial to enroll between 80 and 120 patients with a one-to-one randomization to CRLX101 or standard of care. We currently expect to receive data from this randomized trial by the end of 2015.

Our planned initial indication for CRLX101 in the treatment of renal cell carcinoma is in combination with Avastin in patients who have progressed to a third or fourth line treatment regimen. We estimate that in 2013 approximately 11,000 relapsed renal cell carcinoma patients in the United States became eligible for third line treatment. If we attempt to expand the use of CRLX101 in renal cell carcinoma, we may consider pursuing an approval of CRLX101 for use in combination with Avastin in renal cell carcinoma patients who progress to second line treatment. We estimate that in 2013 there were approximately 21,000 such patients in the United States. In addition, we also may consider pursuing an approval of CRLX101 for use in combination with a TKI in patients receiving their first systemic therapy for renal cell carcinoma. We estimate that in 2013 there were approximately 36,000 such patients in the United States.

Relapsed Ovarian Cancer

Current Treatments for Ovarian Cancer: The American Cancer Society estimated that approximately 22,000 women in the United States would receive a new diagnosis of ovarian cancer in 2013 and that approximately 14,000 women in the United States would die from ovarian cancer in 2013, which would make ovarian cancer the leading cause of death among gynecologic malignancies in the United States.

First-line therapy for ovarian cancer, including epithelial, tubal and peritoneal cancers, is typically inclusive of a platinum and taxane containing therapy with or without Avastin; however, Avastin is not approved for use in ovarian cancer. Some patients will be primary refractory, meaning they never achieve a RECIST-based response to initial therapy; the prognosis for these patients is extremely poor.

The majority of patients with advanced ovarian cancer who achieve a RECIST-based response will eventually experience cancer recurrence. Therapy selected for later-line treatment of patients who achieve a RECIST-based response to frontline therapy depends on whether the patient is defined as platinum sensitive or platinum resistant. Platinum sensitive includes those patients who achieved initial response and whose cancer does not recur for six months or longer after completing platinum-based therapy. Resistant disease includes those who experience recurrence in less than six months. Treatment of patients with platinum-sensitive disease will typically include another platinum containing therapy, usually a doublet where the second agent is a taxane or Gemzar. Alternatively, Doxil (liposomal doxorubicin) may be used. Avastin may also be considered although it is not FDA approved for this indication. Treatment of patients with platinum-resistant disease is more challenging and may include one of several agents, including Avastin, Doxil, topotecan, docetaxel, gemcitabine, weekly paclitaxel and etoposide, none of which have been established to prolong survival. There remains considerable unmet medical need for patients with recurrent ovarian cancer and in particular for those who are platinum resistant.

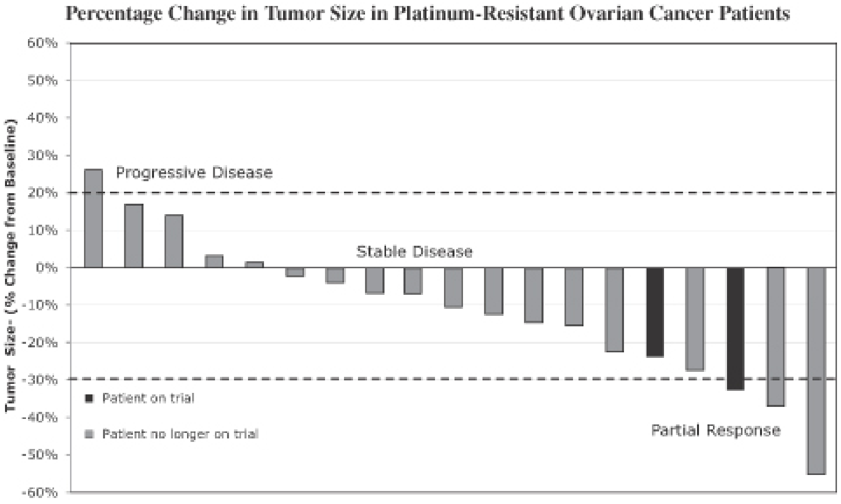
Rationale for use of CRLX101 for Relapsed Ovarian Cancer: Publicly released data from a recently concluded international Phase 3 randomized clinical trial for the treatment of patients with second and third line platinum-resistant ovarian cancer conducted by Hoffman-La Roche revealed that the addition of Avastin to chemotherapy, while displaying notable achievements in progression free survival and a strong trend toward improvements in overall survival in particular patient sub-groups, did not achieve a statistically significant improvement in overall survival among all patients. Based on this and other trials evaluating Avastin use in ovarian cancer, it appears that while benefits of VEGF inhibitors such as Avastin are suggested in this setting, it is unlikely that Avastin will be approved by the FDA for use in ovarian cancer based on the data presented to date. We hypothesize that HIF-1a contributes to resistance to VEGF inhibitors, including Avastin. Furthermore, a comprehensive analysis of over-represented genes in ovarian cancer identifies HIF-1a as a highly active pathway common to both basal breast and serous ovarian cancers and suggests that HIF-1a may be an important therapeutic target in ovarian cancer. As highlighted above, CRLX101 appears to durably suppress HIF-1a and demonstrates notable synergy in combination with VEGF inhibitors, including Avastin, in preclinical tumor models of ovarian cancer. We hypothesize that a CRLX101-mediated override of acquired resistance to Avastin, achieved through the inhibition of HIF-1a, will facilitate the translation of progression free survival and response rate benefits achieved with Avastin in relapsed platinum-resistant ovarian cancer into meaningful and statistically significant overall survival benefits for these patients.

The combination of CRLX101 with Avastin in platinum-resistant ovarian cancer capitalizes on several important aspects of this indication, specifically: ovarian cancer is a HIF overexpressing tumor type, the combination of CRLX101 with Avastin in preclinical ovarian cancer models is synergistic, and CRLX101 and Avastin appear to be well tolerated in humans.

Clinical Development of CRLX101 in Relapsed Ovarian Cancer: A single arm Phase 2 IST of CRLX101 as monotherapy in 29 advanced relapsed ovarian cancer patients is being conducted at Massachusetts General Hospital and affiliated Harvard teaching hospitals in Boston, Massachusetts. The first patient was enrolled in July 2012 and enrollment was completed in July 2013. The primary endpoints of this trial are to achieve progression free survival at six months for at least four patients and to confirm safety and tolerability of CRLX101 dosed at 15mg/m^2 every two weeks in relapsed ovarian cancer patients.

The primary progression free survival endpoint has been met with at least four patients having achieved progression free survival time on trial of six months or longer. In addition, as of March 25, 2014, 15 patients had achieved net tumor shrinkages, with four patients having achieved RECIST-based partial responses. In addition, two patients remained active on trial as of March 25, 2014. In the platinum-resistant patient subpopulation (22 of 29 patients), 19 of 22 patients were receiving CRLX101 as third or later line of therapy, and three of 22 patients received CLRX101 as second line therapy. With 19 platinum-resistant patients evaluable as of March 25, 2014, 18 demonstrated scan results showing stable disease or better for their target legions, with three of these 19 patients having achieved a RECIST partial response.

The graph below shows the change in tumor size for the 19 evaluable platinum-resistant patients in this trial as of March 25, 2014. Each vertical bar in the graph represents the percentage change in tumor size from the time when the patient entered the clinical trial until the largest tumor size reduction or smallest tumor size growth, as applicable, was measured for that patient in accordance with RECIST. The changes in tumor size are unaudited and based on CT-scan assessment performed at the treating center.



These data suggest activity of CRLX101 as monotherapy in relapsed ovarian cancer. Since ovarian cancer has been identified as a HIF overexpressing tumor type and CRLX101 was generally well tolerated in this trial, we are also supporting a combination IST of CRLX101 with Avastin in relapsed platinum-resistant ovarian cancer. This single arm Phase 2 clinical trial of CRLX101 dosed at $15mg/m^2$ every two weeks in combination with Avastin dosed at 10mg/kg every two weeks in second and third line platinum-resistant ovarian cancer patients has been initiated at Massachusetts General Hospital and affiliated Harvard teaching hospitals in Boston, Massachusetts. As of March 25, 2014, two patients have been enrolled. The primary endpoint of the trial is progression free survival at six months in eight patients, and secondary objectives include assessment of response rates and toxicities as assessed by the National Cancer Institute's Common Terminology Criteria for Adverse Events, Version 4.0. A maximum of 43 patients will be enrolled in the trial. Based on the results observed in this trial, including the rates of objective tumor response and progression free survival, we will determine whether to conduct a randomized pivotal trial of the CRLX101-Avastin combination. Based in part on our discussions with our advisory board, we believe that if we observe a 20% or higher objective response rate in the ongoing trial, it will provide a high degree of confidence for success in a subsequent randomized pivotal trial. Therefore, assuming the continued tolerability of the CRLX101-Avastin combination and appropriate signals of objective tumor response and progression free survival activity in the ongoing trial and that we are able to raise adequate additional funds, we expect to initiate the randomized pivotal trial in 2015.

Our planned initial indication for CRLX101 in the treatment of ovarian cancer is in combination with Avastin in platinum-resistant patients who have progressed to a second or third line treatment regimen. We estimate that in 2013 approximately 9,000 relapsed platinum-resistant ovarian cancer patients in the United States became eligible for second or third line treatment. If we attempt to expand the use of CRLX101 in ovarian cancer, we may consider pursuing an approval of CRLX101 for use in combination with Avastin in maintenance therapy. We estimate that in 2013 there were approximately 11,000 such patients in the United States. In addition, we also may consider pursuing an approval of CRLX101 for use in combination with taxanes in patients receiving their first systemic therapy for ovarian cancer. We estimate that in 2013 there were approximately 14,000 such patients in the United States.

Neoadjuvant Rectal Cancer

Current Treatments for Neoadjuvant Rectal Cancer: The American Cancer Society estimated that approximately 40,000 people in the United States would be newly diagnosed with rectal cancer in 2013. According to the American Cancer Society, approximately 28,000 of these people are diagnosed before the disease has metastasized beyond the lymph nodes to one or more distant organs. Patients without distant metastases are candidates for neoadjuvant therapy, which consists of five to six weeks of radiotherapy and chemotherapy, typically Xeloda or 5-FU, which is also referred to as chemoradiotherapy. The goal of chemoradiotherapy is to shrink the tumors as much as possible prior to surgical resection. In clinically manageable treatment therapies that have been evaluated, a pathologic complete response is observed in about 15% to 20% of patients. A pathologic complete response following neoadjuvant chemoradiotherapy is associated with excellent long-term survival versus patients who did not achieve pathologic complete response (five-year odds ratio of 3.28, $p=0.001$), long-term disease free survival (five year odds ratio of 4.33, $p < 0.001$) and lower rates of local recurrence and distant failure.

Since the treatment objective of neoadjuvant chemoradiotherapy followed by surgery is curative, surgeons remove as much tissue as they deem necessary to maximize the chance for a cure. In many cases, this requires the removal of the sphincter together with the cancerous rectal tissue. Patients who achieve a pathologic complete response or significant tumor shrinkage following neoadjuvant chemoradiotherapy often benefit from not having their sphincters removed. This translates into a significantly higher quality of life compared to patients with sphincter removal who will not be able to control their bowel movements for the remainder of their lives. We believe that, in addition to pathologic complete response, sphincter preservation is a compelling and objectively measurable endpoint in the neoadjuvant rectal cancer setting.

Rationale for use of CRLX101 in Neoadjuvant Rectal Cancer: Radiotherapy causes DNA single strand breaks which, if not repaired, lead to desired apoptosis of radiated tumor cells. However, cell repair mechanisms, including topo 1, which re-ligates DNA strand breaks, can undo the radiotherapy damage to tumor cells, thus interfering with the desired effects of the radiotherapy. Since topo 1 is instrumental in repairing radiotherapy-induced DNA single strand breaks, we expect a combinable topo 1 inhibitor to be effective as a radiosensitizer. In fact, combinations of irinotecan plus Xeloda or 5-FU plus radiotherapy have demonstrated pathologic complete response rates between 21% and 37% across various trials, which is greater than the pathologic complete response rates that have been demonstrated across various trials using Xeloda or 5-FU plus radiotherapy. However, the toxicity of irinotecan prevents its addition to this therapy beyond clinical trial settings. CRLX101 in combination with radiotherapy in a head and neck cancer animal model demonstrated notable synergy, which we believe was due to direct anti-cancer effects and enhanced radiosensitization. In addition, local tumor hypoxia is a byproduct of radiotherapy, and there is a well-documented role of hypoxia-induced HIF-1a up-regulation in causing resistance to radiotherapy. Accordingly, we believe that CRLX101, with its durable topo 1 and HIF-1a inhibition, as well as its favorable safety profile, offers strong potential as an add-on drug to standard of care chemoradiotherapy in neoadjuvant rectal cancer.

Clinical Development of CRLX101 in Neoadjuvant Rectal Cancer: A single-arm open-label Phase 1b/2 IST of CRLX101 in combination with Xeloda and radiotherapy in patients with neoadjuvant rectal cancer is being conducted at the University of North Carolina at Chapel Hill and is expected to expand to the University of Indiana and Wake Forest University. This clinical trial is designed to identify the maximum tolerated dose of CRLX101 administered in combination with Xeloda and radiotherapy and to detect signals of increased clinical benefit over Xeloda and radiotherapy alone. The trial is designed to enroll up to 53 patients and has a primary endpoint of pathologic complete response as well as secondary endpoints of disease free survival and overall survival. As of March 25, 2014, two patients have been enrolled in this trial.

Once the maximum tolerated dose is established, we expect to transition into a randomized Phase 2 trial of approximately 80 to 120 patients. This clinical trial will compare the safety and efficacy of CRLX101, Xeloda and radiotherapy to Xeloda and radiotherapy. Two important efficacy endpoints will be measured at the time of surgery: pathologic complete response and sphincter preservation. Assuming the randomized Phase 2 trial is supportive and following discussions with the FDA, we plan to initiate a randomized Phase 3 clinical trial comparing CRLX101, Xeloda and radiotherapy to Xeloda and radiotherapy alone. Based on early assumptions, we expect to enroll approximately 300 to 500 patients in this Phase 3 trial. We expect to conduct the trial as a randomized, well-controlled clinical trial to demonstrate superiority over chemoradiotherapy alone, as measured by the efficacy endpoints of pathologic complete response and sphincter preservation. We believe it is possible that strong efficacy, quality of life and safety data may lead to accelerated approval of CRLX101 in neoadjuvant rectal cancer. As a condition of accelerated approval, we expect that we will need to demonstrate superiority in disease-free survival to confirm approval in this indication.

Assuming completion of the dose-finding portion of the Phase 1b clinical trial by the end of 2014 and that we are able to raise adequate additional funds, we expect to transition into the Phase 2 randomized clinical trial in 2015 and to have pathologic complete response and sphincter preservation data available by late 2015. We expect this data set will provide the foundation for an end of Phase 2 meeting with the FDA to discuss Phase 3 trial design and requirements for accelerated approval, assuming positive pathologic complete response and sphincter preservation data, as well as the requirements to confirm approval in this indication.

Our planned initial indication for CRLX101 in the treatment of rectal cancer is in combination with Xeloda and radiotherapy in patients being treated in the neoadjuvant setting. We estimate that in 2013 approximately 28,000 non-metastatic rectal cancer patients in the United States became eligible for neoadjuvant treatment. If we attempt to expand the use of CRLX101 in rectal cancer, we may consider pursuing an approval of CRLX101 for use in the adjuvant setting. We estimate that in 2013 there were approximately 28,000 such patients in the United States. In addition, we also may consider pursuing an approval of CRLX101 for use in the treatment of first line metastatic colorectal cancer. We estimate that in 2013 there were approximately 29,000 such patients in the United States.

Other indications

Gastric Cancer. A single-arm Phase 2 pharmacodynamic clinical trial of CRLX101 in advanced HER 2 negative gastric cancer patients is being conducted in an IST at the City of Hope National Comprehensive Cancer Center in Duarte, California. The trial objectives are to utilize tumor biopsies to establish differential nanopharmaceutical penetration between tumor and adjacent normal tissue and to establish signals of activity in HER-2 negative gastric cancer patients. The first patient was enrolled in January 2013, and, as of March 25, 2014, evaluable pre- and post-treatment tumor biopsies involving tumor tissue and healthy adjacent tissue have been collected from four patients, three of whom had evaluable biopsies. The biopsies from these three patients have been analyzed for differential drug accumulation between tumor and normal tissue using immunoflourescence techniques. Data from two of these patient-samples measuring camptothecin levels in tumor and adjacent normal tissue between 24 and 48 hours after a single dose of CLRX101 was administered indicated that camptothecin was present in the tumor tissue and very little camptothecin was present in the adjacent normal tissue. We believe these data illustrate dynamic tumor targeting of CRLX101 in patients and confirm in human patients results we have observed in animal tumor models. We believe that this CRLX101 data in humans validates the dynamic tumor targeting properties of our platform.

Small Cell Lung Cancer. A randomized Phase 2 clinical trial of 112 patients comparing CRLX101 as monotherapy to topotecan in advanced small cell lung cancer, or SCLC, is being conducted in an IST at the University of Chicago and at other major medical centers in the United States. The trial objectives are to establish feasibility of enrolling this advanced patient population and to differentiate the safety and efficacy of CRLX101 at 15mg/m^2 dosed every two weeks versus topotecan, the only approved second line SCLC agent. Additionally, we expect the trial may enroll up to 44 patients with chemotherapy-resistant SCLC in a single-arm fashion to receive CRLX101 therapy. The first patient was enrolled in January 2013.

Additional CRLX101 Development Opportunities

We believe that the favorable adverse event profile of CRLX101 may allow combinations with anti-cancer therapies beyond Avastin and Xeloda. This may include combinations with other chemotherapeutics, targeted chemotherapeutics, molecularly targeted agents and nanopharmaceuticals, and may extend CRLX101 into indications beyond our current target indications.

Several approved anti-cancer therapeutics work by reducing blood vessel formation, and thus we believe CRLX101 may be combinable with approved anti-angiogenesis inhibitors other than Avastin, such as Zaltrap, Sutent, Nexavar and Votrient, among others. In preclinical tumor models, in addition to Avastin, we have tested the combination of CRLX101 with Votrient and Zaltrap and have observed synergy between CRLX101 and each of these agents. HIF-1a assays across multiple tumor models have shown CRLX101 to be a durable inhibitor of HIF-1a and to provide synergistic HIF-1a inhibition when combined with Avastin.

Beyond exploiting the apparent synergies from combining topo 1 and HIF inhibition with VEGF inhibition or radiotherapy, as is the focus of our current combination clinical trials, extensive preclinical modeling of CRLX101 combinations with other agents that demonstrate synergistic or additive properties with traditional chemotherapeutic agents, such as taxanes and platinums. These combinations could further enhance the utility of CRLX101 as a backbone agent in combination therapies.

In the future, we may investigate combinations of CRLX101 with poly ADP Ribose Polymerase, or PARP, inhibitors. PARP's main role is to detect and signal single-strand DNA breaks to the enzymatic complex, containing topo 1, that repairs single strand DNA breaks. A combined inhibition of PARP and topo 1 is a synergistic combination that has been well established in preclinical research. To date, the potential of this combination has remained unrealized, as Phase 1 trials of PARP inhibitors and topotecan conducted by others have shown toxicities necessitating dose reductions to sub-therapeutic levels. We believe that, due to its improved toxicity profile as compared to approved topo 1 inhibitors, CRLX101 may be combinable with PARP inhibitors at therapeutically active doses.

CRLX301

Overview

CRLX301 is the nanopharmaceutical analog of CRLX101 with docetaxel as its anti-cancer payload. Docetaxel is a highly active chemotherapeutic that binds to microtubules to trigger cell death in dividing cells. Docetaxel is extensively used in clinical practice and is FDA approved for the treatment of NSCLC, squamous cell carcinoma of the head and neck, hormone refractory prostate cancer, breast cancer and adenocarcinoma. Docetaxel causes toxicities, including death attributable to toxicities, hepatotoxicity, neutropenia, hypersensitivity, severe fluid retention and peripheral neuropathy. These toxicities lead to dose adjustments, treatment discontinuation and extensive supportive care.

Since CRLX301 is an analog of CRLX101, we can utilize a common supply chain, intermediates and manufacturing facilities, thereby creating manufacturing synergies across the two programs. We believe the clinical development risk of CRLX301 is somewhat mitigated because the efficacy of docetaxel in humans is extensively validated. In addition, the safety risk of the nanopharmaceutical is reduced since CRLX101, sharing the identical nanopharmaceutical backbone, has been tested in over 200 patients without serious toxicities attributed to the nanopharmaceutical backbone.

Our target product profile for CRLX301 aims to demonstrate improved efficacy, safety and combinability compared to docetaxel. The potential advantages of CRLX301 would be to increase docetaxel's proven anti-tumor activity by targeting CRLX301 into tumors and sustained release of docetaxel from within tumor cells, thereby achieving sustained drug concentrations in tumor cells. We expect lower systemic exposure with CRLX301 compared to docetaxel, based on preclinical studies, potentially enhancing tolerability.

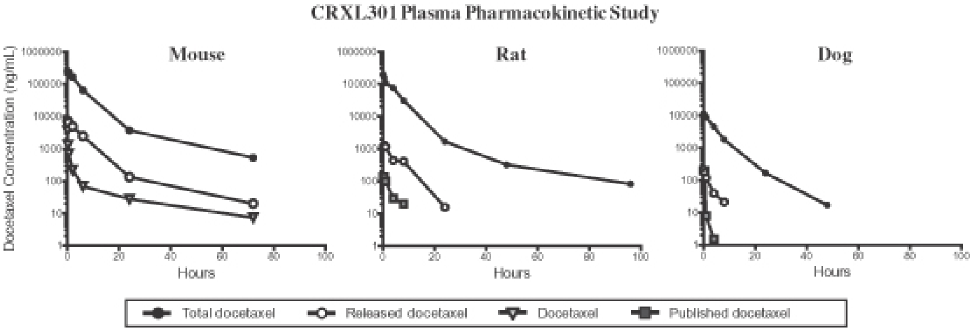
We believe that enhanced therapeutic benefit and a favorable safety profile for CRLX301 would enable combination therapies incorporating CRLX301 with other anti-cancer therapies that may not be combinable today due to docetaxel's toxicities.

CRLX301 Preclinical and IND-Enabling Data

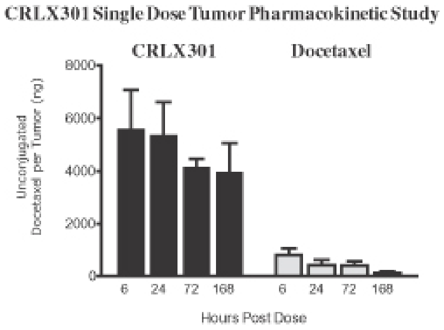
We have conducted the following PK studies in mice, rats and dogs in which CRLX301 demonstrated prolonged circulation as compared to docetaxel:

- a study in which 40 mice were administered a single dose of 15 mg/kg CRLX301 and the PK levels of such mice were compared to the PK levels of 40 mice that received the same dose of docetaxel;
- a study in which 18 rats were administered a single dose of 10 mg/kg CRLX301 and the PK levels of such rats were compared to the PK of docetaxel obtained from published data in rats that received the same dose of docetaxel; and
- a study in which six dogs were administered a single dose of 0.75 mg/kg CRLX301 and the PK levels of such dogs were compared to the PK of docetaxel obtained from published data in dogs that received the same dose of docetaxel.

In each of these studies, the concentrations of docetaxel, total and unconjugated, were measured using liquid chromatography/tandem mass spectrometry. As illustrated in the graphs below, plasma concentration of docetaxel in the mice following dosing of CRLX301 was prolonged, lacked a rapid distribution phase and resulted in an approximately 500-fold increase in plasma exposure of total drug compared to docetaxel in mice treated with docetaxel. We also observed similar increases in exposure when we compared CRLX301 PK data to published data for docetaxel in dog and rat, also as illustrated in the graphs below.

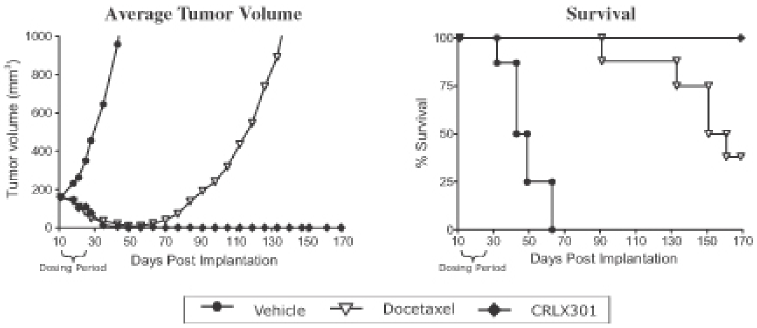


We have also measured tumor levels of CRLX301 that were approximately ten-times the tumor levels of docetaxel in a mouse tumor PK study. We measured concentrations of docetaxel in mice following administration of a single dose of either CRLX301 or docetaxel in mice, in which certain mouse melanoma tumor cells were implanted subcutaneously and allowed to establish tumors. After administration of a single dose of 15 mg/kg docetaxel or 15 mg/kg CRLX301, tumors were extracted from the mice at various time points up to one week post-administration, frozen and homogenized, and unconjugated docetaxel concentrations were measured using liquid chromatography/tandem mass spectrometry. These data were then multiplied by the tumor weight to estimate the amount of docetaxel delivered to the tumor. As shown in the figure below, approximately ten times the amount of docetaxel released from CRLX301 was detected in tumors of the mice that were dosed with CRLX301 as compared to the mice that were dosed with the same amount of docetaxel.



We tested the anti-tumor activity of CRLX301 in animal xenograft models of prostate cancer, squamous non-small cell lung cancer, adenocarcinoma non-small cell lung cancer, ovarian cancer, multi-drug resistant ovarian cancer, triple-negative breast cancer and in a syngeneic melanoma model. In all of these models, CRLX301 was either superior or comparable to docetaxel in either delay of tumor progression and/or complete response rate.

In one such study, we treated nude mouse xenograft models in which human DU-145 prostate cancer tumor cells were implanted subcutaneously into mice and allowed to establish tumors. We administered 30 mg/kg of CRLX301, 30 mg/kg of docetaxel or saline (vehicle) by intravenous infusion. Each dose group consisted of eight animals, and all mice were treated weekly for three weeks. Both CRLX101 and docetaxel delayed tumor growth and improved survival rates as compared to the saline-treated mice, but only CRLX301-treated mice displayed complete tumor regression and 100% tumor-free survival at the conclusion of the study. These results are illustrated in the graphs below and are representative of the other animal xenograft models tested. In all such models, we observed longer lasting or equivalent tumor growth inhibition and higher or equivalent survival rates with CRLX301 as compared to docetaxel.



These preclinical studies were not designed to demonstrate a statistically significant effect of treatment with CLRX301 as compared to treatment with docetaxel. Nonetheless, in three of the seven animal xenograft models we conducted, CRLX301 demonstrated superior tumor growth inhibition, which was statistically significant (in each case, p<.05). CRLX301 also demonstrated a statistically significant survival advantage in four of these seven animal xenograft models (in each case, p<.05) and was associated with longer survival in the three animal xenograft models in which CRLX301 did not demonstrate a statistically significant survival advantage.

We have conducted Good Laboratory Practice, or GLP, toxicology studies in 148 rats and 32 dogs that revealed similar target organ effects for CRLX301 as compared to docetaxel; however, the maximum tolerated dose for CRLX301 was approximately 20% higher compared to published data of the maximum tolerated dose for docetaxel in dogs. We observed no evidence of platform-based toxicities. The higher maximum tolerated dose for CRLX301 and a greater than 50-fold reduced volume of distribution in plasma PK studies in rats and dogs are consistent with a decreased systemic exposure of CRLX301 compared to published data for docetaxel, as measured by a volume of distribution that is 50 and 138 times lower for rats and dogs, respectively.

Clinical Development of CRLX301

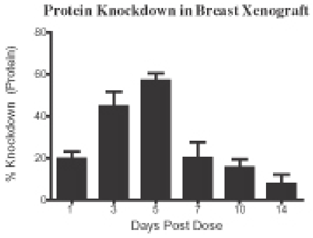
In our clinical development of CRLX301, we plan focus on the utility of this nanopharmaceutical to provide effective delivery of docetaxel into tumors for prolonged periods of time with reduced systemic exposure, enhancing anti-tumor activity while potentially reducing the toxicity observed with traditional taxanes. We intend to commence the Phase 1 portion of a Phase 1/2a clinical trial at two cancer centers in Australia by late 2014. This clinical trial will allow first-in-human dosing of CRLX301 in patients with advanced solid tumor malignancies in order to evaluate the safety of the drug and establish a maximum tolerated dose. Patients in this Phase 1 portion of the clinical trial will receive an intravenous infusion of CRLX301 on day one of a 21-day cycle and continue treatment every three weeks until progression of disease or excessive toxicity is observed. Tumor response evaluations will be performed using RECIST guidelines, and patients will be considered evaluable for efficacy if at least one dose of study drug is received.

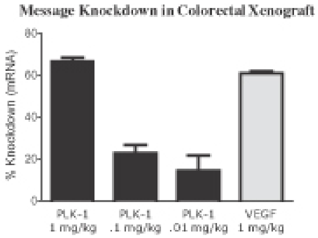
Phase 1 patients will be enrolled in a standard three-plus-three dose escalation format. Enrollment in a particular dosing cohort will be halted when two or more out of six patients in a cohort experience a dose-limiting toxicity during cycle one following initiation of study drug. The maximum tolerated dose will be defined as the highest dosing level in which fewer than two out of six patients experience a dose-limiting toxicity during cycle one of therapy. Up to 36 evaluable patients may be enrolled in these Phase 1 dose escalation cohorts, with the exact number being dependent on the actual number of patients per cohort and the number of cohorts investigated.

After we begin Phase 1 clinical testing in Australia, we intend to submit an IND to the FDA, which will allow us to add two cancer centers in the United States to the clinical trial, as the clinical trial transitions from a Phase 1 trial to a Phase 2a trial. The Phase 2a portion of the trial will enroll an additional 24 to 30 patients so that CRLX301 can be evaluated at the maximum tolerated dose established in the Phase 1 portion of the trial in two or three tumor types of interest. Tumor types of interest will be determined based on biological rationale, clinical need, regulatory path, commercial opportunity and results observed during the Phase 1 portion of the trial. For clinical development of CRLX301, we expect to choose from among those tumor types in which docetaxel is approved and active, in which docetaxel is not approved but where taxanes have demonstrated efficacy or in which resistance to prior taxanes has been established. Such possible tumor types include, among others, breast cancer, prostate cancer, ovarian cancer, melanoma and head and neck cancer. In addition, once we have established a maximum tolerated dose, we may choose to conduct a randomized Phase 2 clinical trial in a pre-identified lead indication of interest in order to conduct a head-to-head comparison of CRLX301 against the standard of care in this tumor type of interest. In such a scenario, we expect CRLX301 would be evaluated in approximately 80 patients, randomized one to one between CRLX301 and standard of care.

RNA Delivery

Preclinical data have shown that siRNA therapeutics in oncology are hampered by a short circulation time and poor tumor uptake. A longer circulating, tumor targeting siRNA delivery system could have the ability to translate promising siRNA science into useful cancer drugs. We have shown in animal tumor models that our PNP technology allows the differential delivery of intact siRNA into tumor cells by stabilizing the RNA inside the nanoparticles, prolonging circulation and increasing tumor uptake, leading to prolonged knockdown in tumors. Our preclinical data demonstrates tumor specific uptake of siRNA containing PNPs leading to significant knock-down in tumors across five different tumor models covering four different tumor types (colorectal, hepatic, ovarian and breast) using four different target genes. For example, we have achieved specific knock-down of green fluorescent protein, or GFP, in nude mouse xenograft models in which human breast cancer tumor cells expressing GFP were implanted subcutaneously in mice and allowed to establish tumors. Following a single administration into the tail vein of anti-GFP containing 3 mg/kg siRNA PNPs, knock-down of GFP protein was observed for at least one week, peaking at approximately 60% knock-down five days post-treatment. In addition, when we administered PNPs containing siRNA against polo-like kinase 1, or PLK-1, a proto-oncogene that drives cell cycle progression, or VEGF, a signal protein produced by cells that stimulates vasculogenesis and angiogenesis, to colorectal tumor bearing mice, we also observed approximately 65% and 60% knock-down of messenger RNA, or mRNA, levels, respectively, measured 24 hours after each of three daily intravenous treatments of 1 mg/kg siRNA PNPs. We continued to observe knockdown of PLK-1 mRNA at 0.1 and 0.01 mg/kg siRNA PNPs in the same study. These results are shown in the graphics below.


Protein Knockdown in Breast Xenograft


Message Knockdown in Colorectal Xenograft

We have tested our siRNA containing PNPs in mice and have established a favorable safety profile, allowing us to deliver high amounts of siRNA without the incidence of serious adverse effects in the animal tumor models. Human complement pathways are not activated, and we do not see a cytokine response as a result of siRNA containing PNP administration in mice.

If our platform is able to improve RNA delivery into tumor cells, we believe this would be valuable to companies that are pursuing RNA-based therapeutic approaches in oncology. We do not have the expertise to identify, select, secure and manufacture proprietary anti-cancer RNAs that would be delivered using our platform. Accordingly, we do not intend to focus our business on RNA-based therapeutic approaches, and we would seek to explore this aspect of our platform in collaboration with companies that have expertise in RNA-based therapeutic approaches.

Competition

The biopharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. These competitors also compete with us in recruiting and retaining top 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.

Due to the large unmet medical need, global demographics and relatively attractive reimbursement dynamics, the oncology market is fiercely competitive. In each indication we are pursuing, there are approved cancer therapeutics and agents under clinical development for use as monotherapy and combination therapy. Each of the top ten global pharmaceutical companies and most of the mid-size pharmaceutical companies has a strong research and development and commercial presence in oncology. Smaller companies also focus on oncology, including companies such as ARIAD Pharmaceuticals, Inc., Agios Pharmaceuticals, Inc., BIND Therapeutics, Inc., Clovis Oncology, Inc., Endocyte, Inc., Epizyme, Inc., ImmunoGen, Inc., Incyte Corporation, Infinity Pharmaceuticals, Inc., MacroGenics, Inc., Merrimack Pharmaceuticals, Inc., OncoMed Pharmaceuticals, Inc., Onconova Therapeutics, Inc., Pharmacyclics, Inc., Puma Biotechnology, Inc., Seattle Genetics, Inc. and TESARO, Inc.

Several companies are marketing and developing oncology products. Companies with marketed nanopharmaceutical oncology products include Celgene Corporation (Abraxane (nab-paclitaxel) indicated for breast cancer, NSCLC and pancreatic cancer) and Spectrum Pharmaceuticals (Marqibo (vincristine sulfate liposome injection) indicated for relapsed Philadelphia chromosome-negative acute lymphoblastic leukemia). Companies with nanopharmaceutical oncology product candidates in clinical development include BIND Therapeutics, Inc. (BIND 014 for NSCLC and metastatic castration-resistant prostate cancer), Celator Pharmaceuticals, Inc. (CPX-351 for acute myeloid leukemia), Celsion Corporation (ThermoDox (lyso-thermosensitive liposomal doxorubicin) for solid tumors), Cytimmune Sciences, Inc. (CYT-6091 for oncology and autoimmune diseases) and Supratek Pharma Inc. (SP1049C for solid tumors). In addition, at least two companies have oncology product candidates in clinical development that are camptothecin reformulations: Merrimack Pharmaceuticals' liposomal irinotecan (MM-398 for pancreatic and colorectal cancer) and Nektar Therapeutics' etirinotecan pegol (NKTR102 for breast cancer).

We believe CRLX101 is the only non-nucleotide oncology product candidate in clinical development that targets the HIF pathway. Santaris Pharma A/S has a Locked Nucleic Acid oncology product candidate that targets HIF-1a (SPC-2968, which was referred to as EZN-2968 when it was being developed by Enzon Pharmaceuticals, Inc.). In addition, there are drugs and biologics in development that could compete with CRLX101 in each of its lead indications: relapsed renal cell carcinoma, relapsed ovarian cancer and neoadjuvant rectal cancer.

In relapsed renal cell carcinoma, the six FDA-approved therapies commonly used for treatment represent only two mechanistic classes—those that target VEGF signaling, including TKIs, and mTORIs—and there are no approved cytotoxic drugs. In relapsed ovarian cancer, there are multiple approved drugs and multiple companies developing therapeutic candidates in various stages of development. For example, OncoMed Pharmaceuticals is developing demcizumab, and Roche is developing DMOT4039A. 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.

In neoadjuvant rectal cancer, Xeloda, which is marketed by Roche, was approved for use in rectal cancer in 2005. Xeloda is used in the neoadjuvant setting in combination with radiotherapy, and this chemo-radiotherapeutic regimen represents the current standard of care in the United States. CRLX101 is being developed as a combination agent to be used with radiotherapy and Xeloda. In neoadjuvant rectal cancer, we are only aware of one competitor: Isofol Medical is developing a molecule that is currently labeled [6R] 5,10-methylenetetrahydrofolate.

Several companies are developing taxane-containing nanoparticles for oncology that are competitors to CRLX301. For example, BIND Therapeutics Inc.'s BIND-014 is a docetaxel containing nanoparticle in active clinical development. Nippon Kayaku's NK105 is a paclitaxel micelle nanoparticle in late stage clinical development for breast and stomach cancer. Drug-polymer conjugated nanoparticles are also being developed, such as Nektar Therapeutics' NKTR-105.

The key competitive factors affecting the success of all our therapeutic product candidates, if approved, are likely to be their efficacy, safety, dosing convenience, price, the level of generic competition and the availability of reimbursement from government and other third party payors.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to protect, for example, the technology platforms used to generate our product candidate, related technologies and/or other aspects of the inventions that are important to our business. We also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We plan to continue to expand our intellectual property estate by filing patent applications directed to dosage forms, methods of treatment and additional compositions created or identified from our platform and ongoing development of our product candidates. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; maintain our licenses to use intellectual property owned by third parties; preserve the confidentiality of our trade secrets; and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen, and maintain our proprietary positions.

A third party may hold intellectual property, including patent rights that are important or necessary to the development of our product candidates or use of our platform. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings which may result in further narrowing or even cancellation of patent claims. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Any patents that we own or license may be challenged, narrowed, circumvented or invalidated by third parties.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine priority of invention.

Patents

Our patent portfolio includes issued patents and pending applications worldwide. These patents and applications fall into three broad categories: (1) covalent linkage of therapeutic agents to a cyclodextrin-containing polymer, or CDP, as in CRLX101 and CRLX301; (2) association of a therapeutic agent to a polymer and (3) polymeric nanoparticles which can be used to deliver various types of therapeutic agents including large molecules.

Cyclodextrin Polymer (CDP) Platform Technology: Covalent Linkage of Therapeutic Agent to Cyclodextrin-Containing Polymer: CRLX101 and CRLX301

We own through an assignment from Calando, or exclusively license from Caltech, 13 patent families generally related to CDPs and/or to linear CDP-therapeutic agent conjugates (CDP-agent conjugates), including CRLX101 and CRLX301, methods of delivering the CDP-agent conjugates, methods of making the CDP-agent conjugates and methods of treating various disorders by administering the CDP-agent conjugates. These patent families include 18 issued United States patents and 25 issued foreign counterparts, as well as over 19 pending United States patent applications and over 54 pending foreign applications. These patents and applications, if issued, generally will expire between 2018 and 2034. These patent families include:

- One family of patents and patent applications licensed from Caltech claiming linear cyclodextrin-containing polymers, methods of making the polymers, compositions containing the polymers, and methods of delivering the compositions (one issued United States patent expires in 2018 and foreign counterparts, where issued, expire in 2019). Foreign counterparts are issued and/or pending in other major markets, including Europe, China and Japan, as well as several other countries;
- One family of Cerulean-owned patents and patent applications claiming linear cyclodextrin-containing polymers and CDP-agent conjugates and formulations, methods of delivering and methods of making CDP-agent compositions, CRLX101 composition of matter and formulations, methods of delivering and methods of making the CRLX101 compositions, composition of matter and formulations relating to CRLX301, and methods of delivering and methods of making the compositions relating to CRLX301 (issued United States patents expire in 2023 or 2024 and foreign counterparts, where issued, expire in 2023). This family was assigned to us pursuant to our agreements with Calando. Foreign counterparts are issued and/or pending in other major markets, including Europe, China and Japan, as well as several other countries;
- Three families of Cerulean-owned patent applications claiming methods of treating disorders, including cancers such as ovarian cancer and colorectal cancer (e.g., rectal cancer) by administering CRLX101, alone or in combination with other therapeutic agents (e.g., angiogenesis inhibitors) at selected doses and dosing schedules (United States patents and foreign counterparts would, if issued, expire between 2030 and 2034). One of these three families of Cerulean-owned patent applications was assigned to us under our agreements with Calando. Foreign counterparts for at least some of these families are pending in other major markets, including Europe, China and Japan, as well as several other countries;
- Three families of Cerulean-owned patent applications claiming methods of treating various disorders, including, for example, cancer and inflammatory disorders, by administering CDP-agent conjugates, including for example, CRLX101 and CRLX301 and other CDP-agent conjugates (United States patents and foreign counterparts would, if issued, expire in 2031 or 2033). Foreign counterparts for at least some of these families are pending in other major markets, including Europe, China and Japan, as well as several other countries;
- One family of Cerulean-owned patent applications claiming CDP-taxane conjugate compositions of matter, including compositions relating to CRLX301, and methods of treating disorders, including cancer, by administering such a CDP-taxane conjugate alone or in combination with other therapeutic agents, at selected doses and dosing schedules (United States patents and foreign counterparts would, if issued, expire between 2030 and 2032). Foreign counterparts are pending in other major markets, including Europe, China and Japan, as well as several other countries; and
- Four families of Cerulean-owned patent applications claiming technology relating to potential future product candidates, including CDP conjugates in which other therapeutic agents such as epothilones, proteosome inhibitors, peptides, and janus kinase inhibitors are covalently linked to the linear cyclodextrin-containing polymer (United States patents and foreign counterparts would, if issued, expire between 2030 and 2034). One of these four families of Cerulean-owned patent applications was assigned to us under our agreements with Calando.

Additional CDP Platform Technology: Association of Therapeutic Agent to Polymer

We own through an assignment from Calando, or exclusively license from Caltech and Calando, six patent families generally directed to supramolecular complexes that include linear cyclodextrin-containing polymers and therapeutic agents where the polymers are cross-linked, e.g., with cross-linking agents. These patent families include over eight issued United States patents and over 11 issued foreign counterparts, as well as, over five United States patent applications and several foreign applications. These patents and patent applications, if issued, generally will expire between 2019 and 2030. These patent families include:

- One family of patents and patent applications licensed from Caltech claiming supramolecular complexes of linear cyclodextrin-containing polymers and therapeutic agents wherein the polymers are cross-linked, e.g., with cross-linking agents, and methods of making and delivering the supramolecular complexes (one issued United States patent expires in 2018 and foreign counterparts expire in 2019). A foreign counterpart patent issued in Europe; no other foreign protection is being pursued;
- One family of patents and patent applications licensed from Calando and Caltech claiming compositions that include the following components: (1) a cyclodextrin-containing polymer, (2) a complexing agent which includes a moiety that forms an inclusion complex with the cyclodextrin in the linear cyclodextrin-containing polymer and is covalently linked to a stabilizer or agent that increases solubility of the composition, a ligand which is covalently linked to the stabilizer or agent which increases solubility of the composition; and (3) a therapeutic agent, and methods of making these compositions and methods of treating patients by administering the compositions (issued United States patents expire between 2021 and 2022 and foreign counterparts, where issued, expire in 2021). Foreign counterparts are issued and/or pending in other major markets, including China and Japan, as well as several other countries;
- Three families of patents and patent applications licensed from Calando claiming compositions comprising polynucleotides and cyclodextrin-containing polymers, and methods for the delivery of polynucleotides with a cyclodextrin-containing polymer (issued United States patents expire between 2026 and 2030 and foreign counterparts, where issued, expire between 2022 and 2029); and
- One family of Cerulean-owned patents and patent applications claiming polymer compositions that include a (1) linear biocompatible polymer with a plurality of inclusion hosts, (2) linking molecules, each linking molecule comprising moieties that form inclusion complexes with the inclusion hosts, and (3) at least one therapeutic agent covalently attached to a moiety that forms an inclusion complex with the inclusion hosts, wherein the linking molecules cross-link the polymer solely through inclusion complexes (one issued United States patent expires in 2028 and any additional United States patents, if issued, would expire in 2023; we are not pursuing foreign protection for this family).

Polymeric Nanoparticles (PNP) Platform Technology: Small and Large Molecule Delivery

We own, or exclusively license from MIT, 12 patent families which generally relate to nanoparticles containing selected polymers linked to a therapeutic agent or another molecule. These patent families include 17 United States patent applications and 37 foreign applications. These patent applications, if issued, generally will expire between 2025 and 2034. These patent families include:

- Two families of patent applications licensed from MIT claiming nanoparticles containing selected polymers covalently linked to a therapeutic agent and nanometer-sized vehicles that include radionuclides for use in diagnostics (United States patents, if issued, would expire in 2025 or 2026 and foreign counterparts, if issued, would expire in 2025) A foreign counterpart for one of these families is pending in Europe;
- One family of Cerulean-owned patent applications claiming nanoparticles that include polymer-therapeutic agent conjugates, amphiphilic polymers and surfactants (United States patents and foreign counterparts, if issued, would expire in 2030). Foreign counterparts are pending in other major markets, including Europe, China and Japan, as well as several other countries ;

- Three families of Cerulean-owned patent applications claiming nanoparticles that include various combinations of polymer-therapeutic agent conjugates, amphiphilic polymers, cationic moieties and surfactants wherein the therapeutic agent is a nucleic acid agent (e.g., siRNA, mRNA, antisense molecule) and their use in nucleic acid delivery (United States patents and foreign counterparts, if issued, would expire between 2031 and 2034). Foreign counterparts for at least some of these families are pending in other major markets, including Europe, China and Japan, as well as several other countries;
- One family of Cerulean-owned patent applications claiming nanoparticles that include various combinations of polymer-therapeutic agent conjugates, amphiphilic polymers, cationic moieties and surfactants wherein the therapeutic agent is a polypeptide (United States patents and foreign counterparts, if issued, would expire in 2031) Foreign counterparts are pending in other major markets, including Europe, China and Japan, as well as several other countries ;
- Two families of Cerulean-owned patents and patent applications claiming PNPs that include therapeutic agents such as epothilones and proteosome inhibitors that are covalently linked to the polymers contained in the PNP (United States patents, if issued, would expire in 2030; we are not pursuing foreign protection for this family); and
- Three families of Cerulean-owned patents and patent applications claiming optimized PNP formulations that include the use of cyclic oligosaccharides as lyoprotectants, PNP platform technology to treat various disorders such as neurological and metabolic disorders, and optimized methods of making PNPs (United States patents, if issued, would expire between 2031 and 2033 and foreign counterparts would expire in 2033).

Patent Term

The base term of a United States patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a United States patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO. In some cases, the term of a United States patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

The term of a United States patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one United States patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug, and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, have analogous patent term extension provisions which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products, their methods of use, and/or methods of manufacture.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We typically rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. For example, significant elements of the making and formulating of our products are based on trade secrets and know-how that are not publicly disclosed. We protect trade secrets and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements provide that all confidential information developed or made known during the course of an individual or entity's relationship with us must be kept confidential during and after the relationship. These agreements also provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties.

Trademarks

We also seek trademark protection in the United States and in foreign jurisdictions where available and when appropriate. The name "CERULEAN" is a registered trademark in the United States, Australia, the European Union, Israel, Japan, South Korea, Liechtenstein, Mexico, Norway, Russia, Singapore, Switzerland, Turkey, and the Ukraine and is covered by pending applications for trademark registration in Canada, China, and India. The trademark is solely owned by Cerulean Pharma Inc, in the field of pharmaceutical preparations as well as in the field of diagnostic and prognostic preparations. The Cerulean logo is a registered trademark in the United States and is solely owned by Cerulean Pharma Inc. CERULEAN and the Cerulean logo is a registered trademark in Mexico and is solely owned by Cerulean Pharma Inc. The term "Leadership in Nanopharmaceuticals" is a registered trademark in the United States and is solely owned by Cerulean Pharma Inc. The term "Making Nanopharmaceuticals Big" is covered by a pending United States trademark application and is solely owned by Cerulean Pharma Inc. The symbol ™ indicates a common law trademark. Other service marks, trademarks and trade names appearing in this prospectus are the property of their respective owners.

Assignments and In-License Agreements

Calando Pharmaceuticals, Inc.

In June 2009, we entered into two agreements with Calando, the CRLX101 Agreement and the Platform Agreement, each of which we subsequently amended. Under these agreements, Calando assigned and licensed to us certain assets. These assets include the clinical asset then known as IT-101, later renamed CRLX101, and rights to Calando's cyclodextrin system for purposes of conjugating or complexing certain other therapeutic agents to the system.

CRLX101 Agreement:

Under the CRLX101 Agreement, we obtained certain rights to CRLX101. As noted below in the description of the Platform Agreement, Calando also assigned to us certain patents and patent applications, including, with respect to composition of matter and methods of use, for CRLX101. In addition, under the CRLX101 Agreement, Calando transferred ownership of the CRLX101 IND to Cerulean. Also, under the CRLX101 Agreement, Calando initially granted to us a worldwide, royalty bearing, exclusive (even as to Calando) license, with the right to grant sublicenses, to Calando's interest under certain patents, patent applications, and know-how owned or controlled by Calando, to research, develop, make, have made, use, market, offer to sell, distribute, sell and import CRLX101 formulated for intravenous, intrarterial, intrathecal and/or intraperitoneal therapy, to treat and/or prevent disease in humans. As noted below in the description of the Caltech Agreement, all of the patents, patent applications and know-how that were initially licensed to us by Calando under the CRLX101 Agreement and upon which CRLX101 is dependent are now directly licensed to us by Caltech, and we retained the license described above from Calando for patents, patent applications and know-how that are directed to other aspects of the cyclodextrin system but on which CRLX101 is not dependent. For purposes of our obligations to Calando under the CRLX101 Agreement, we treat the intellectual property licensed to us by Caltech as if it were still licensed to us by Calando. These licensed and assigned patent rights are described in more detail above under "Intellectual Property."

Under the CRLX101 Agreement, we are obligated to use commercially reasonable efforts to develop CRLX101 throughout the world and, following the first commercial sale of CRLX101 in a particular country, to make CRLX101 commercially available in such country.

Upon entering the CRLX101 Agreement, we paid Calando approximately $1.3 million, which included the purchase of CRLX101 drug substance and drug product inventory. If we achieve certain development and sales events with CRLX101, we are obligated to pay milestone payments which could total, in the aggregate, $32.8 million. If we or one of our affiliates sells CRLX101, we are also required to pay tiered royalty payments ranging from low-to mid-single digits, depending on whether or not there is patent protection for CRLX101 at the time of sale as a percentage of worldwide net sales. Our royalty payment obligations in a particular country begin on the date of first commercial sale of CRLX101 in that country and end on the later of ten years from the date of first commercial sale of CRLX101 in that country or the expiration of all patents licensed to us by Caltech or Calando, referred to as Licensed Patent Rights, or assigned to us by Calando, referred to as the Assigned Patent Rights, which cover CRLX101 in that country. With respect to CRLX 101 that is developed and sold by an unaffiliated third party to whom we grant a license or sublicense under any of 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 sublicense income that we are obligated to pay Calando is in the low- to mid-double digits, and varies depending on the stage of development of CRLX101 at the time that we first provide or receive draft terms of a license arrangement with the third party that results in a license arrangement, unless the negotiations terminate, in which case the percentage depends on the development stage of CRLX 101 when the negotiations restart.

We have the first right to enforce the Licensed Patent Rights and Assigned Patent Rights, other than one subset of licensed patents on which CRLX101 is not dependent, which Calando has the sole right to enforce.

We and Calando are required to indemnify each other for losses and expenses in connection with any third party claims arising out of the indemnifying party’s breach of the CRLX101 Agreement, the negligence or willful misconduct of the indemnifying party or its affiliates or sublicensees under the CRLX101 Agreement or any product liability arising out of CRLX101 developed, made, used or sold by or on behalf of the indemnifying party or its affiliates or sublicensees.

The CRLX101 Agreement will remain in effect until the expiration of all of our royalty obligations to Calando. We also have the right to terminate the CRLX101 Agreement for any reason on thirty days prior notice to Calando, in which case, unless we certify that the termination was due to specified safety concerns with CRLX101, we will grant Calando an exclusive (even as to Cerulean), royalty-free license, under the Assigned Patent Rights, to research, develop, make, have made, use, market, offer to sell, distribute, sell and import CRLX101, we will assign the IND for CRLX101 to Calando and, if consistent with our business plans, we will discuss granting Calando a license under know-how that we developed that relates to CRLX101. If we fail to meet our diligence obligations under the CRLX101 Agreement after a specified cure period, the license may convert to a non-exclusive license and we will have to grant Calando a non-exclusive license under the Assigned Patent Rights to research, develop, make, have made, use, market, offer to sell, distribute, sell and import CRLX101. If the license is converted to a non-exclusive license, the royalties payable to Calando will be reduced by a specified percentage. If we fail to meet our payment obligations under the agreement and are unable to cure such failure within specified time periods, Calando can terminate the agreement, we are obligated to grant Calando an exclusive (even as to Cerulean), royalty-free license, under the Assigned Patent Rights to research, develop, make, have made, use, market, offer to sell, distribute, sell and import CRLX101 and to assign the IND for CRLX101 to Calando, resulting in our loss of rights to CRLX101. If we or one of our affiliates challenges the validity or enforceability of any of the licensed patents, Calando has the right to terminate the agreement. For any breach of the CRLX101 Agreement not described above, the non-breaching party’s sole remedy if such breach is not cured within a specified time period is to seek money damages from the breaching party.

Platform Agreement:

Under the Platform Agreement, Calando assigned to us the Assigned Patent Rights and granted to us a worldwide, royalty bearing, exclusive (even as to Calando) license, with the right to grant sublicenses, to Calando’s interest under certain patents, patent applications, and know-how owned or controlled by Calando

(a) to conduct research and development on the cyclodextrin system, including making improvements thereto, in order to research, develop, make, have made, use, market, offer to sell, distribute, sell and import CDP-based Products and (b) to research, develop, make, have made, use, market, offer to sell, distribute, sell and import CDP-based Products. The field of the license is the treatment and/or prevention of disease in humans. CDP-based Products are defined as products conjugated or complexed to the cyclodextrin system, other than any products containing cytolysin, tubulysin, certain second generation epothilones or a nucleic acid, which we refer to as Retained Products, and CRLX101, which is covered by the CRLX101 Agreement described above. Under the Platform Agreement, we are obligated to use commercially reasonable efforts to develop CDP-based Products throughout the world and, following the first commercial sale of CDP-based Product in a particular country, to make CDP-based Product commercially available in such country. These exclusively licensed patent rights, as well as patent rights assigned to us pursuant to the agreement, are described in more detail above under “Intellectual Property.”

Upon entering the Platform Agreement, we paid to Calando approximately $1.2 million, which included the payment for assignment of the Assigned Patent Rights and cyclodextrin-containing polymers and precursor inventory. We granted Calando a worldwide, royalty-free, exclusive (even as to Cerulean), perpetual and irrevocable license, with the right to grant sublicenses, under the Assigned Patent Rights to research, develop, make, have made, use, market, offer to sell, sell and import the Retained Products.

If we achieve certain development and sales events with respect to any CDP-based Product, we are obligated to pay milestone payments which could total, in the aggregate, $18.0 million per CDP-based Product. If we or one of our affiliates sells a CDP-based Product, we are also required to pay tiered royalty payments ranging from low-to mid-single digits, depending on whether or not there is patent protection at the time of sale, as a percentage of worldwide net sales. Our royalty payment obligations in a particular country begin on the first date of first commercial sale of the CDP-based Product in that country and end on the later of ten years from the date of first commercial sale of that CDP-based Product in that country or the expiration of all patents licensed or assigned from Calando which cover that CDP-based Product in that country. With respect to a CDP-based Product that is developed and sold by a third party to whom we grant a license or sublicense under any of the intellectual property that we licensed from Calando or that Calando assigned to us, 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 sublicense income that we are obligated to pay Calando does not exceed the low double digits.

We have the first right to enforce the licensed patent rights and the Assigned Patent Rights, other than one subset of licensed patents which Calando has the sole right to enforce.

We and Calando are required to indemnify each other for losses and expenses in connection with any third party claims arising out of the indemnifying party’s breach of the Platform Agreement, the negligence or willful misconduct of the indemnifying party or its affiliates or sublicensees under the Platform Agreement or any product liability arising out of a CDP-based Product developed, made, used or sold by or on behalf of the indemnifying party or its affiliates or sublicensees. Calando also indemnifies us for losses and expenses in connection with any third party claim arising out of a Retained Product developed, made, used or sold by or on behalf of Calando or its affiliates or licensees.

The Platform Agreement will remain in effect until the expiration of all of our royalty obligations to Calando. We also have the right to terminate the Platform Agreement for any reason on thirty days prior written notice to Calando, in which case we will grant Calando an exclusive (even as to Cerulean), royalty-free license, under Assigned Patent Rights, to research, develop, make, have made, use, market, offer to sell, distribute, sell and import the CDP-based Products and, if consistent with our business plans, we would discuss granting Calando a license under know-how that we developed that relates to the cyclodextrin system or CDP-based Products. If we fail to meet our diligence obligations under the agreement after a specified cure period, Calando may convert the license to a non-exclusive license and we will have to grant Calando a non-exclusive license under the Assigned Patent Rights to research, develop, make, have made, use, market, offer to sell, distribute, sell and import CDP-based Products. If the license is converted to a non-exclusive license, the royalties payable to Calando will be reduced by a certain percentage. If we fail to meet our payment obligations under the agreement and are unable to cure such failure within specified time periods, Calando can terminate the agreement, resulting in our loss of rights to the CDP-based Products and an obligation to grant Calando an exclusive (even as to Cerulean), royalty-free license, under the Assigned Patent Rights to research, develop, make, have made, use, market, offer to sell, distribute, sell and import CDP-based Products. If we or one of our affiliates challenges the validity or enforceability of any of the licensed patents, Calando has the right to terminate the agreement. For any breach of the Platform Agreement not described above, the non-breaching party's sole remedy if such breach is not cured within a specified time period is to seek money damages from the breaching party.

California Institute of Technology

Certain of the patents, patent applications, and know-how licensed to us under the CRLX101 Agreement and the Platform Agreement were licensed to Calando by the California Institute of Technology, or Caltech, pursuant to an agreement entered into between Calando and Caltech in May 2000 and subsequently amended, which we refer to as the Calando/Caltech Agreement. In August 2013, we entered into an agreement with Calando and Caltech under which Calando terminated its rights and obligations under the Calando/Caltech Agreement and Caltech agreed to directly honor the exclusive license, including the right to grant further sublicenses, granted to us by Calando under the Caltech intellectual property formerly licensed to Calando.

We are obligated to pay Caltech minimum annual royalties and the costs it incurs to prosecute and maintain the licensed patent rights. We may offset those prosecution and maintenance costs against any milestones or royalties that we owe to Calando under the CRLX101 Agreement or the Platform Agreement.

Following the earlier of our receipt of notice from Calando that it has made certain payments to third parties or the first anniversary of the first commercial sale of a product covered by the Caltech patent rights, we will directly pay to Caltech the amounts that it would have been entitled to receive from Calando with respect to our sales of the licensed products, and we will pay to Calando the remainder of the royalties we owe them under the CRLX101 Agreement and the Platform Agreement.

We have the first right to enforce the Caltech licensed patent rights.

We may terminate our rights and obligations to Caltech and Calando with respect to any of the Caltech licensed intellectual property either in its entirety or as to any jurisdiction or as to any part of the intellectual property upon a specified period of prior notice to Caltech and Calando. Caltech has the right to terminate the agreement if we fail to make a payment, or otherwise materially breach the agreement, and fail to cure such breach within specified grace periods.

Massachusetts Institute of Technology

In December 2006, we entered into an exclusive license agreement with MIT, which we refer to as the MIT Agreement. The MIT Agreement has been amended four times, including to extend or suspend the time period for achieving certain diligence milestones, and the most recent amendment was entered into in August 2013. Under the MIT Agreement, we have a worldwide exclusive license, with the right to grant sublicenses, in all human and veterinary therapeutic and diagnostic areas, under certain patent rights owned by MIT, to develop, make, have made, use, sell, offer to sell, lease and import products covered by the licensed patent rights, and to develop and perform licensed processes. These exclusively licensed patent rights are described in more detail above under "Intellectual Property."

We are required to use commercially diligent efforts to develop licensed products or licensed processes, to introduce licensed products or licensed processes into the commercial market and thereafter to make licensed products or licensed processes reasonably available to the public. By March 1, 2015, we are required to present MIT with a plan, satisfactory to MIT, to develop the licensed products and a proposal for specific diligence terms for licensed products. We and MIT will then negotiate in good faith the diligence terms, but if we and MIT are unable to agree to such diligence terms by the end of June 2015, MIT will have the right, in its sole discretion, to terminate the agreement. If, prior to the end of June 2015, MIT becomes aware that another party with whom we are not in active negotiations wishes to obtain a license under the patent rights and we have not yet submitted a satisfactory development plan to MIT, MIT will request a development plan from us and from the other party, and MIT will select either our development plan or the other party's development plan based on MIT's determination of which plan is in the best interests of commercializing the licensed patents. If MIT selects the other party's development plan, MIT may, in its sole discretion, terminate the exclusive license agreement with us, limit our field of use under the exclusive license agreement, or convert our exclusive license to a non-exclusive license.

Under the MIT Agreement, as of December 31, 2013, we had paid MIT approximately $0.5 million in the aggregate, consisting of annual maintenance fees and reimbursement of patent-related fees incurred by MIT, and we issued a certain number of shares of our common stock to MIT and individuals affiliated with MIT. We are obligated to pay MIT annual license maintenance fees that escalate beginning in January 2015. We are also obligated to pay royalties at a low single digit percentage of net sales of licensed products or licensed processes by us, our affiliates or our sublicenses. We are also required to pay a percentage, in the low double digits, of the payments we receive from our sublicensees which are attributable to the granting of a sublicense under the licensed patents, subject to certain exclusions.

MIT retains the right to practice the licensed patent rights for research, teaching and educational purposes. We may not assert the licensed patents against any non-profit entity using the licensed patents for research purposes not benefitting a for-profit entity.

Any of the licensed patent rights claiming inventions that were funded by the government are subject to certain rights retained by the United States government under a law commonly called the Bayh-Dole Act. These rights include, among other things, a royalty-free, non-exclusive license for the United States government to practice these inventions. Any products used or sold in the United States and covered by these patents must be substantially manufactured in the United States, unless a waiver is obtained from the U.S. government.

MIT controls prosecution and maintenance of the licensed patents. We are responsible for all costs associated with filing, prosecuting and maintaining the licensed patent rights. As long as our license remains exclusive, we have the first right to enforce the licensed patents against infringers in the licensed field.

We are required to indemnify MIT for any liabilities and expenses in connection with any claims concerning any licensed product, process or service under the MIT Agreement.

We have the right to terminate the agreement for any reason by providing MIT with a specified amount of prior written notice. MIT has the right to terminate the agreement if we cease to carry on our business related to the agreement, if we fail to pay any amounts due and payable under the agreement, subject to a grace period, or if we materially breach the agreement and fail to cure such breach within specified grace periods. The MIT Agreement otherwise terminates, on a country-by-country basis, upon the expiration or abandonment of all licensed patents and patent applications.

The Research Foundation of State University of New York on behalf of University at Buffalo

In August 2007, we entered into an exclusive license agreement with The Research Foundation of State University of New York on behalf of University at Buffalo, which we refer to as the SUNY Agreement. The SUNY Agreement has been amended four times, including to extend the time period for achieving certain diligence milestones, and the most recent amendment was entered into in September 2013. Under the SUNY Agreement, we have a worldwide, royalty bearing, exclusive license, with the right to grant sublicenses, for the treatment and/or prevention of disease in humans, under certain patent rights owned by SUNY, to research, develop, make, have made, use, offer for sale, sell, have sold, import and export certain products covered by the licensed patent rights. These exclusively licensed patent rights are described in more detail, as specified in the SUNY Agreement, above under "Intellectual Property."

We are required to diligently proceed with the research, development, manufacture, use and sale of licensed products under the agreement, to use commercially reasonable efforts to commercialize and market licensed products as soon as practicable, and to make licensed products available on commercially reasonable terms once introduced into the marketplace. In particular, we are required to fulfill specific development and regulatory milestones by particular dates and, during each calendar year prior to the first commercial sale of a licensed product, spend a specified amount on the research, development or commercialization of licensed products or precursor technologies or products, and if we fail to do so SUNY may elect to increase our license maintenance fee and, in the case of a second failure, our exclusive license will be converted to a non-exclusive license.

Under the SUNY Agreement, as of December 31, 2013, we had paid SUNY approximately $0.2 million in the aggregate, consisting of an upfront license fee, a field-of-use expansion fee, annual maintenance fees and reimbursement of patent-related fees incurred by SUNY. We are also obligated to pay SUNY an escalating annual license maintenance fee and development milestone payments which could total, in the aggregate, less than $0.1 million and royalties in the low single digits as a percentage of net sales by us, our affiliates or our sublicensees of licensed products.

SUNY retains the right to practice the licensed patent rights for educational purposes and internal research and development, including collaborations with researchers at other academic and non-profit research institutions. Any of the licensed patent rights claiming inventions that were funded by the government are subject to certain rights retained by the United States government under a law commonly called the Bayh-Dole Act. These rights include, among other things, a royalty-free, non-exclusive license for the United States government to practice these inventions. Any products used or sold in the United States and covered by these patents must be substantially manufactured in the United States, unless a waiver is obtained from the U.S. government.

SUNY controls prosecution and maintenance of the licensed patents, although we have an approval right over certain actions. We reimburse SUNY for all reasonable costs associated with filing, prosecuting and maintaining the licensed patent rights. SUNY has the first right to enforce the licensed patents against infringers in the licensed field. We have the right to enforce the licensed patents if SUNY does not institute an infringement action within a specified period of time.

We are required to indemnify SUNY for any claims and expenses resulting from the exercise or practice of the license granted to us, including liabilities arising from the production, manufacture, sale, use, lease or advertisement of the licensed products.

The SUNY Agreement will remain in effect until the expiration of all licensed patents and patent applications, unless we elect to earlier terminate the entire license, or the license with respect to certain patent families, subject to providing SUNY with a specified amount of prior written notice. SUNY has the right to terminate the SUNY Agreement if we have a bankruptcy action filed against us, have a receiver appointed for us, or if we materially breach the agreement, and fail to cure such situation or breach within a specified grace period. The SUNY Agreement will automatically terminate if we cease to carry on our business, file for bankruptcy, become insolvent, make an assignment for the benefit of creditors, or we challenge the validity or enforceability of any of the licensed patents.

Manufacturing

We currently contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for commercial manufacturing, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers. Although we rely on contract manufacturers, we have personnel with manufacturing experience to oversee our relationships with contract manufacturers.

Our contract manufacturers have manufactured what we believe to be sufficient quantities of CRLX101 drug product to support clinical trials in through the first half of 2015, and we will begin manufacturing in 2014 for additional supply to continue clinical development of CRLX101 for the second half of 2015 and beyond. The current drug substance and drug product manufacturing processes for CRLX101 are scaled to support phase 2/3 clinical development under current Good Manufacturing Practice, or cGMP, standards, and we believe are adequate to support further development and scale up for commercial demand at a reasonable cost of goods. While we believe that our existing supplier of drug substance is capable of producing drug substance in commercial quantities, we have also identified a new third party manufacturer capable of providing commercial quantities of drug product. If we are unable to arrange for third-party manufacturing with this or other alternative vendors, or fail to do so on commercially reasonable terms, we may not be able to successfully produce and market CRLX101.

Processes for producing CRLX301 have been developed and used successfully to produce drug substance and drug product for GLP safety studies. These processes are currently being used to produce cGMP supplies for Phase 1 clinical development.

Both CRLX101 and CRLX301 include complicated polymer backbone structures as well as cytotoxic agents. Although these characteristics may limit alternative third party manufacturers, we believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, and we have or are pursuing back-up suppliers for certain stages of the manufacturing process. We cannot be certain, however, that identifying and establishing relationships with additional alternate sources, if necessary, would not result in significant delay or material additional costs.

Sales and Marketing

We intend to build the commercial infrastructure in the United States necessary to effectively support the commercialization of CRLX101, if approved, and future oncology products, if approved. The commercial infrastructure for specialty oncology products typically consists of a targeted, specialty sales force that calls on a limited and focused group of physicians supported by sales management, internal sales support, an internal marketing group and distribution support. Additional capabilities important to the oncology marketplace include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, oncology group networks and government accounts.

Based on the number of physicians who treat renal cell carcinoma, ovarian, and rectal cancer and the size of competitive sales forces, we believe that we can effectively target the relevant U.S. market with a focused sales force. If CRLX101 is approved in additional indications, we might need to increase the number of representatives. To develop the appropriate U.S. commercial infrastructure, we will have to invest significant amounts of financial and management resources.

In the future, we may utilize one or more strategic partners to optimally commercialize CRLX101 and our other products globally.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export, of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources and the successful outcome of those processes cannot be guaranteed.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or DOJ or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA’s good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product’s identity, strength, quality and purity;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease (e.g. cancer) or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Investigator Sponsored Trials

Investigator sponsored trials are clinical trials where the investigator of the trial is also the "sponsor" of the trial for regulatory purposes. An "investigator" conducts clinical investigations and is the person under whose immediate direction the study drug is administered or dispensed to patients. A "sponsor" initiates and takes responsibility for a clinical investigation. A person who both initiates and conducts a clinical trial, and is responsible for all regulatory requirements, is designated as a "sponsor-investigator" by the FDA. Clinical investigators at academic medical centers who initiate clinical trials with a lawfully marketed drug to be used in a patient population or indication not within the official labeling often fit within this designation. In addition, as is the case with our investigator-sponsored trials, a company may provide a sponsor-investigator with supply of its unapproved product candidate and funding for the trial. Investigators who initiate and conduct such trials are responsible for obtaining an IND from the FDA and for ensuring compliance with the IND and associated regulatory requirements. As provided by the FDA's regulations, the sponsor of a clinical trial is responsible for, among other things, selecting qualified investigators, providing them with the information they need to conduct the trial properly, ensuring proper monitoring of the trial, ensuring that the trial is conducted in accordance with the protocols contained in the IND, maintaining an effective IND with respect to the trial, and ensuring that the FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug. In contrast, in a company-sponsored trial, the pharmaceutical company whose drug will be studied is the sponsor of the trial and, as such, is responsible for ensuring compliance with all regulatory requirements, including obtaining the IND.

In connection with our ongoing investigator sponsored trials of CRLX101, we have entered into agreements with the institutions at which the trials are being conducted. The terms of these agreements are customary and generally provide that (a) the institution is responsible for obtaining and maintaining any necessary IND for the trial, for conducting the trial in accordance with an agreed upon protocol and applicable regulatory requirements and for safety reporting to us and the FDA, (b) the institution grants to us a license to use the trial data for any legally permissible purpose and assigns to us all intellectual property rights relating to the trial drug developed during the course of the agreement, (c) we are responsible for supplying the trial drug and making agreed upon payments to the institution to fund the trial and (d) the term of the agreement is the duration of the applicable trial, however, the agreement can be terminated for convenience with notice, upon the request of an applicable regulatory agency, for safety reasons or following an uncured material breach by the other party.

Section 505(b)(2) NDAs

NDAs for most new drug products generally are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA’s previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application “were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.”

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA’s previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product’s chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently exceeding $2.1 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $104,000 per product and $554,000 per establishment. These fees are typically increased annually.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA’s receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections usually cover all facilities associated with an NDA submission, including drug component manufacturing (such as Active Pharmaceutical Ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a risk evaluation and mitigation strategy or REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy and Priority Review

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as “breakthrough therapies.” A product may be designated as a breakthrough therapy if it is intended, either 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 product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA’s goal for taking action on a marketing application from ten months to six months after the application is accepted for filing.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

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. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug[.]”

Upon approval of an ANDA, the FDA indicates whether the generic product is “therapeutically equivalent” to the RLD in its publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” also referred to as the “Orange Book.” Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA’s designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. In cases where 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, as discussed below, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30 Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, a NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity, which is discussed below. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States. A company must request orphan product designation before submitting a NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of a NDA, plus the time between the submission date of a NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a drug under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state’s assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Data and Market Exclusivity in the European Union

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator’s data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator’s data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the drug if such company can complete a full MAA with a complete database of pharmaceutical test, preclinical tests and clinical trials and obtain marketing approval of its product.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal healthcare 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 either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- 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 false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Health Care Reform Law will require manufacturers of drugs, devices, drugs and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party 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 in addition to requiring drug manufacturers to report information related to payments to physicians and other health care 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.

Employees

As of February 28, 2014, we had 21 full-time employees, including a total of 10 employees with M.D. or Ph.D. degrees. Of our workforce, 14 employees are engaged in research and development. None of our employees is represented by labor unions or covered by collective bargaining agreements.

Facilities

Our principal facilities consist of approximately 14,200 square feet of research and office space located on the 5th Floor of 840 Memorial Drive, Cambridge, Massachusetts. The lease expires in February 2016, subject to our option to extend the lease for an additional two years.

Legal Proceedings

We are not currently a party to any material legal proceedings.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the name, age and position of each of our executive officers and directors as of March 1, 2014.

Name	Age	Position
Oliver S. Fetzer, Ph.D.	49	President, Chief Executive Officer and Director
Edward G. Garmey, M.D.	46	Senior Vice President and Chief Medical Officer
Christopher D. T. Guiffre, J.D.	45	Senior Vice President and Chief Business Officer
Karen L. Roberts	57	Senior Vice President, Finance and Administration
Alan L. Crane	50	Chairman of the Board
Paul A. Friedman, M.D.(2)(3)	71	Director
Steven E. Hall, Ph.D.(1)(2)	59	Director
William T. McKee(1)	52	Director
William H. Rastetter, Ph.D.(1)(3)	65	Director
Ram Sasisekharan, Ph.D.	49	Director
Robert I. Tepper, M.D.(2)	58	Director

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(1) Member of audit committee.
(2) Member of compensation committee.
(3) Member of nominating and corporate governance committee.

Oliver S. Fetzer, Ph.D. has served as our President and Chief Executive Officer and as a member of our board of directors since 2009. From 2004 until 2007, Dr. Fetzer served as Senior Vice President, Corporate Development and Research & Development at Cubist Pharmaceuticals, Inc., or Cubist. From 2003 to 2004, he served as Cubist's Senior Vice President, Corporate Development and Chief Business Officer and, from 2002 until 2003, he served as its Senior Vice President, Business Development. Before his time at Cubist, commencing in 1993, Dr. Fetzer held various positions of increasing responsibility at the Boston Consulting Group, or BCG, a global leading management consulting firm, including Consultant, Project Leader, Principal and Partner and Managing Director. Since 2005, Dr. Fetzer has served on the board of directors of Auxilium Pharmaceuticals, Inc., a public specialty biopharmaceutical company, and since 2011 on the board of directors of Tecan Group AG, a public provider of laboratory instruments and solutions in biopharmaceuticals, forensics and clinical diagnostics. He received a B.S. in Biochemistry from the College of Charleston, his Ph.D. in Pharmaceutical Sciences from the Medical University of South Carolina and an M.B.A. from Carnegie Mellon University. We believe that Dr. Fetzer is qualified to serve on our board of directors because of his years of service as our Chief Executive Officer and his extensive knowledge of our company and industry.

Edward G. Garmey, M.D. has served as our Senior Vice President and Chief Medical Officer since 2011. Prior to joining Cerulean, Dr. Garmey held a variety of positions at ArQule, Inc., a clinical-stage biotechnology company, including as Vice President for Clinical Development since 2008, and as Clinical Development Liaison from 2007 to 2008. From 2006 to 2007, Dr. Garmey served as Medical Director at GPC Biotech, a German biopharmaceutical company and now a subsidiary of Agennix AG, where he helped oversee global clinical development studies. Dr. Garmey received his A.B. from Harvard University and his M.D. from New York University. He is a member of the Scientific Advisory Board for the Harvard-MIT Broad Institute's Cancer Vaccine Initiative.

Christopher D. T. Guiffre, J.D. has served as our Senior Vice President and Chief Business Officer since 2012. Prior to that, Mr. Guiffre held a number of senior executive positions at various biopharmaceutical companies. From 2010 to 2012, he served as President and Chief Executive Officer of Alvos Therapeutics, Inc., a private biotechnology company subsequently acquired by Arrowhead Research Corp.; from 2008 to 2009, he served as Chief Business Officer at Hydra Biosciences, Inc., a private biopharmaceutical company; and from

2001 to 2008, he served as a senior executive at Cubist Pharmaceuticals, Inc., most recently as Senior Vice President, General Counsel and Secretary. From 1997 to 2001, Mr. Guiffre held several positions at Renaissance Worldwide, Inc., including Vice President, General Counsel and Clerk. Prior to that, he was an Associate at Bingham McCutchen LLP. He received a B.S. degree from Babson College, a J.D. from Boston College Law School and an M.B.A. from Boston College Carroll School of Management.

Karen L. Roberts has served as our Senior Vice President, Finance and Administration since 2010. Prior to joining Cerulean, from 2001 to 2009, Ms. Roberts served as Vice President, Finance and Administration of Elixir Pharmaceuticals, Inc., a biopharmaceutical company where she was the senior financial executive responsible for all aspects of finance, accounting and administration. From 1998 to 2001, Ms. Roberts served in a number of roles, including Corporate Controller and Chief Accounting Officer and Vice President, Finance, at Frontline Group, Inc., a provider of business performance improvement services and products. Prior to that, Ms. Roberts served as Director of Finance at Dyax Corp., a biotechnology company, and as Corporate Controller and Director Financial Administration at T Cell Sciences, Inc., a biopharmaceutical company. Ms. Roberts received her B.S. in Business Administration with a concentration in accounting from Salem State College.

Alan L. Crane is one of our co-founders and has served as a member of our board of directors since 2006 and our chairman since 2009. From our founding until 2009, Mr. Crane served as our Chief Executive Officer. Currently, he is a general partner at Polaris Partners and was a Venture Partner at Polaris from 2002 until 2009. From 2002 until 2006, Mr. Crane was President and Chief Executive Officer of Momenta Pharmaceuticals, Inc. Prior to this, he was Senior Vice President of Global Corporate Development at Millennium Pharmaceuticals, Inc., where he was responsible for leading Millennium’s strategic partnering, mergers and acquisitions, and licensing activities. Mr. Crane serves on the boards of privately held life sciences companies Visterra, Inc., T2 Biosystems, Inc., Ocular Therapeutix, Inc., Seventh Sense Biosystems, Inc., Calorics Pharmaceuticals, Inc., XTuit Pharmaceuticals, Inc. and Vaccinex, Inc. Previously, he served on the boards of Sirtris Pharmaceuticals, Inc. (acquired by Glaxo SmithKline), Adnexus Therapeutics, Inc. (acquired by Bristol Myers Squibb), and Hydra Biosciences. Mr. Crane received his B.A., M.A. and M.B.A. from Harvard University. We believe that Mr. Crane is qualified to serve on our board of directors due to his role in our founding, his institutional knowledge as a result of his continuous service on our board since 2006, and his significant experience as an investor in, and executive and director of, life sciences companies.

Paul A. Friedman, M.D. has served as a director since January 2014. From 2001 to January 2014, he was Chief Executive Officer of Incyte Corporation, a public biotechnology company, and he served as President of Incyte from 2004 to January 2014. From 1998 until 2001, Dr. Friedman was President of DuPont Pharmaceuticals Research Laboratories, a wholly owned subsidiary of DuPont Pharmaceuticals Company (formerly The DuPont Merck Pharmaceutical Company), from 1994 to 1998 he served as President of Research and Development of The DuPont Merck Pharmaceutical Company, and from 1991 to 1994 he served as Senior Vice President at Merck Research Laboratories. Prior to his work at Merck and DuPont, Dr. Friedman was an Associate Professor of Medicine and Pharmacology at Harvard Medical School. Dr. Friedman is a Diplomate of the American Board of Internal Medicine and a Member of the American Society of Clinical Investigation. Dr. Friedman is a director of Incyte, public biopharmaceutical companies Auxilium Pharmaceuticals, Inc. and Durata Therapeutics, Inc. and private biopharmaceutical company Gliknik, Inc. Dr. Friedman was a director of Bausch & Lomb Incorporated from 2004 until its acquisition in 2007 and was a director of Sirtris Pharmaceuticals, Inc. from March 2008 until its acquisition in June 2008. Dr. Friedman received his A.B. from Princeton University and his M.D. from Harvard Medical School. We believe that Dr. Friedman is qualified to serve on our board of directors due to his management and research and development experience and his experience serving on the boards of life sciences companies.

Steven E. Hall, Ph.D. has served as a member of our board of directors since 2010. Dr. Hall has served as a venture partner at Lilly Ventures, the venture capital arm of Eli Lilly and Company, since 2009. Prior to joining Lilly Ventures, from 2003 to 2008, Dr. Hall was Senior Vice President, Research and Development, at Serenex, Inc., a biotechnology company (acquired by Pfizer), where he was also a co-founder. From 1994 to 2003, Dr. Hall held multiple positions, including Site Director, Sphinx Labs, Eli Lilly where he oversaw lead generation efforts in the areas of combinatorial chemistry, automation, high-throughput screening, biomolecular research, and information technology. Dr. Hall is the author of more than 40 papers and 60 patents. He received his B.S. in chemistry from Central Michigan University and his Ph.D. in organic chemistry from Massachusetts Institute of Technology. Dr. Hall currently sits on the boards of privately held life sciences companies FORMA Therapeutics, Inc., Esanex, Inc., Nimbus Discovery, LLC and Hydra Biosciences, Inc., and on the board of crowdsourcing service provider InnoCentive, Inc. We believe that Dr. Hall is qualified to serve on our board of directors due to his broad experience in the life sciences industry as a venture capitalist, director and senior executive and his research knowledge.

William T. McKee has served as a director since January 2014. Mr. McKee served as Chief Operating Officer and Chief Financial Officer at EKR Therapeutics, Inc., a private specialty pharmaceutical company, from 2010 until 2012 when EKR was sold to Cornerstone Therapeutics Inc., a public pharmaceutical company. Until 2010, Mr. McKee served as the Executive Vice President and Chief Financial Officer of Barr Pharmaceuticals, LLC, a subsidiary of Teva Pharmaceutical Industries Limited, a generic pharmaceutical company, and the successor entity to Barr Pharmaceuticals, Inc., a public specialty pharmaceutical company, which was acquired by Teva in 2008. Mr. McKee was also Executive Vice President and Chief Financial Officer of Barr prior to its acquisition by Teva, after having served in positions of increasing responsibility at Barr from 1995 until its acquisition. Prior to joining Barr, Mr. McKee served as Director of International Operations and Vice President-Finance at Absolute Entertainment, Inc., a private developer and marketer of entertainment software, from 1993 until 1994. From 1990 until 1993, Mr. McKee worked at Gramkow & Carnevale, CPA’s, an accounting firm, and from 1983 until 1990, he worked at Deloitte & Touche. Mr. McKee serves on the board of directors of Auxilium Pharmaceuticals, Inc., a public specialty biopharmaceutical company. Mr. McKee received his B.B.A. from the University of Notre Dame. We believe that Mr. McKee is qualified to serve on our board of directors due to his financial and leadership experience as a chief financial officer and a certified public accountant.

William H. Rastetter, Ph.D. has served as a director since January 2014. He is a Co-Founder of Receptos, Inc., a biopharmaceutical company, where he has been a director and Chairman of the Board since May 2009 and was Acting Chief Executive Officer from May 2009 to November 2010. Dr. Rastetter served as a Partner at the venture capital firm of Venrock Associates from 2006 to February 2013. Prior to his tenure with Venrock, Dr. Rastetter was Executive Chairman of Biogen Idec, from the merger of the two companies (Biogen and Idec Pharmaceuticals) in 2003 through the end of 2005. He joined Idec Pharmaceuticals in 1986 and served as Chairman and Chief Executive Officer. Prior to Idec, he was Director of Corporate Ventures at Genentech, Inc. and served as well in a scientific capacity at Genentech. Dr. Rastetter also serves as the Chairman of public life sciences companies Illumina, Inc., Neurocrine Biosciences, Inc. and Fate Therapeutics Inc. and as a director of Regulus Therapeutics, Inc., a public biopharmaceutical company. Dr. Rastetter has held various faculty positions at the Massachusetts Institute of Technology and Harvard University and is an Alfred P. Sloan Fellow. Dr. Rastetter holds a B.S. in Chemistry from the Massachusetts Institute of Technology and received his M.A. and Ph.D. in Chemistry from Harvard University. We believe Dr. Rastetter is qualified to serve on our board of directors due to his extensive experience in the biotechnology industry, his broad leadership experience with Idec Pharmaceuticals, Inc. and on several public and private biotechnology company boards, and his experience with financial matters.

Ram Sasisekharan, Ph.D. is one of our co-founders and has served as a consultant and as a member of our board of directors since 2006. Dr. Sasisekharan has been a Professor of Biological Engineering at the Massachusetts Institute of Technology since 1996 and is Director of the Harvard-MIT Division of Health Sciences & Technology and Edward Hood Taplin Professor of Biological Engineering & Health Sciences & Technology and also a member of the Koch Institute for Integrative Cancer Research. Dr. Sasisekharan founded Momenta Pharmaceuticals, Inc. and Visterra, Inc., and he serves on the board of directors of Visterra, Inc. Dr. Sasisekharan’s research on complex polysaccharides has led to over 125 publications and over 50 patents, including the core technologies of Momenta Pharmaceuticals, Inc. He has won both the Burroughs Wellcome and Beckman Foundation Young Investigator Awards and was the recipient of the 1998, 1999, 2000 and 2001

CaPCure Awards from the CaPCure Foundation. Dr. Sasisekharan serves on the steering committee of the Consortium for Functional Glycomics. Dr. Sasisekharan received his B.S. in Physical Sciences from Bangalore University, his M.S. in Biophysics from Harvard University and his Ph.D. in Medical Sciences from Harvard Medical School. We believe Dr. Sasisekharan is qualified to serve on our board of directors due to his experience in science and research and his institutional knowledge as a result of his continuous service on our board since 2006.

Robert I. Tepper, M.D. has served as a member of our board of directors since 2006. Dr. Tepper has over 25 years of experience building and operating leading research and development operations. Dr. Tepper co-founded Third Rock Ventures, L.P. in March 2007 and focuses on the formation, development and scientific strategy of its portfolio companies, as well as actively identifying and evaluating new investments. Prior to joining Third Rock Ventures, L.P., from 2003 to 2007, Dr. Tepper served as President of Research and Development at Millennium Pharmaceuticals, Inc. Before joining Millennium Pharmaceuticals, Inc. in 1994, he served as principal investigator in the laboratory of tumor biology at Massachusetts General Hospital Cancer Center. Dr. Tepper is also a founder and former member of the scientific advisory board of Cell Genesys/Abgenix. Dr. Tepper holds an A.B. in biochemistry from Princeton University and an M.D. from Harvard Medical School. Dr. Tepper serves as an adjunct faculty member at Harvard Medical School and Massachusetts General Hospital and is an advisory board member of several leading healthcare institutions, including the Partners HealthCare Center for Personalized Genetic Medicine, Harvard Medical School and Tufts Medical School. Dr. Tepper is a board member of private life sciences companies Alcresta, Inc., Allena Pharmaceuticals, Inc., Constellation Pharmaceuticals Inc. and Kala Pharmaceuticals, Inc. as well as public biopharmaceutical company bluebird bio Inc., and is also on the board of overseers at Tufts University. We believe that Dr. Tepper is qualified to serve on our board of directors due to his experience in the venture capital industry, particularly with biotech and pharmaceutical companies, combined with his experience building and operating research and development operations, on the boards of public and private life sciences companies and as faculty and advisory board members of several healthcare institutions.

Board Composition and Election of Directors

Our board of directors currently consists of eight members, three of whom are designated by certain of our preferred stockholders and elected pursuant to a voting agreement that we have entered into with the holders of our preferred stock and certain of our other stockholders. The voting agreement will terminate upon the closing of this offering and there will be no further contractual obligations regarding the election of our directors. Following the closing of this offering, in accordance with the terms of our certificate of incorporation and bylaws that will become effective as of the closing of this offering, our board of directors will be divided into three classes: class I, class II and class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows:

- the class I directors will be Dr. Sasisekharan and Dr. Tepper, and their term will expire at the annual meeting of stockholders to be held in 2015;
- the class II directors will be Mr. Crane, Dr. Fetzer and Dr. Hall, and their terms will expire at the annual meeting of stockholders to be held in 2016; and
- the class III directors will be Dr. Friedman, Mr. McKee and Dr. Rastetter, and their terms will expire at the annual meeting of stockholders to be held in 2017.

Upon the expiration of the term of a class of directors, directors in that class are eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires. In accordance with the terms of our certificate of incorporation and bylaws that will become effective upon the closing of this offering, the authorized number of directors may be changed only by resolution of the board of directors, our directors may be removed only for cause by the affirmative vote of the holders of 75% or more of our voting stock and any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Under applicable NASDAQ rules, a director will only qualify as an "independent director" if, in the opinion of our board of directors, such director does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. Our board of directors has determined that all of our directors, other than Dr. Fetzer and Mr. Crane, are independent directors, as defined by the applicable NASDAQ rules. In making such determination, the board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that the board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director.

There are no family relationships among any of our directors or executive officers.

Lead Independent Director

Our board of directors has appointed Dr. Rastetter to serve as our lead independent director. As lead independent director, Dr. Rastetter presides over periodic meetings of our independent directors, serves as a liaison between our Chairman and the independent directors and performs such additional duties as our board of directors may otherwise delegate.

Board Committees

Our board has established three standing committees—audit, compensation, and nominating and corporate governance—each of which operates under a charter that has been approved by our board of directors. Current copies of each committee's charter are posted on the Corporate Governance section of our website, www.ceruleanrx.com. The composition of each committee will be effective upon the closing of this offering.

Our board has determined that all of the members of our audit committee, the compensation committee and the nominating and corporate governance committee satisfy the independence standards for such committees established by the SEC and the NASDAQ listing rules, as applicable. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

Audit committee

The members of our audit committee are Drs. Hall and Rastetter and Mr. McKee. Mr. McKee chairs the audit committee. Upon the closing of this offering, the audit committee's responsibilities will include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function;
- discussing our risk management policies;
- establishing policies regarding hiring employees from the registered public accounting firm and procedures for the receipt, retention and treatment of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, registered public accounting firm and management;

- reviewing and approving or ratifying our policies and procedures for related person transactions and review and approve or ratify all related person transactions; and
- preparing the audit committee report required by SEC rules to be included in our proxy statement for our annual meeting of stockholders.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Mr. McKee is an “audit committee financial expert” as defined by applicable SEC rules.

Compensation committee

The members of our compensation committee are Drs. Tepper, Hall and Friedman. Dr. Tepper chairs the compensation committee. Upon the closing of this offering, the compensation committee’s responsibilities will include:

- reviewing and approving, or making recommendations to our board with respect to, the compensation of our executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board with respect to director compensation;
- reviewing and discussing annually with management our “Compensation Discussion and Analysis”; and
- preparing the annual compensation committee report required by SEC rules.

Nominating and corporate governance committee

The members of our nominating and corporate governance committee are Drs. Rastetter and Friedman. Dr. Rastetter chairs the nominating and corporate governance committee. Upon the closing of this offering, the nominating and corporate governance committee’s responsibilities will include:

- recommending to our board the persons to be nominated for election as directors and to each of the board’s committees;
- reviewing and making recommendations to the board with respect to management succession planning;
- developing and recommending to the board corporate governance guidelines; and
- overseeing an annual evaluation of the board.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serves as a member of the board of directors or compensation committee or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee is, or has ever been, an officer or employee of our company.

Code of Ethics and Code of Conduct

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of the code on our website, www.ceruleanrx.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

EXECUTIVE COMPENSATION

This section describes the material elements of our executive compensation for our "named executive officers" and the most important factors relevant to an analysis of these policies. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers named in the "Summary Compensation Table" below, or our "named executive officers," and is intended to place in perspective the data presented in the following tables and the corresponding narrative. Our "named executive officers" for 2013 are Oliver S. Fetzer, our President and Chief Executive Officer, Christopher D.T. Guiffre, our Senior Vice President and Chief Business Officer, and Edward Garmey, our Senior Vice President and Chief Medical Officer.

In preparing to become a public company, we have begun a thorough review of all elements of our executive compensation program, including the function and design of our equity incentive programs. We have begun, and expect to continue in the coming months, to evaluate the need for revisions to our executive compensation program to ensure that our program is competitive with the companies with which we compete for executive talent and is appropriate for a public company.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers during our fiscal year ended December 31, 2013.

Name and Principal Position	Salary ($)	Bonus ($)(1)	Option Awards ($)(2)	All Other Compensation ($)	Total ($)
Oliver S. Fetzer, Ph.D. *President and Chief Executive Officer*	352,000	176,000	146,088	10,968(3)	685,056
Christopher D.T. Guiffre, J.D. *Senior Vice President and Chief Business Officer*	295,000	73,750	—	10,968(3)	379,718
Edward Garmey, M.D. *Senior Vice President and Chief Medical Officer*	303,000	75,750	—	10,968(3)	389,718

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(1) The amounts reported in the "Bonus" column reflect, for each named executive officer, the amount of bonus compensation that was earned in 2013, which will be paid in March 2014.

(2) The amounts reported in the "Option Awards" column reflect the aggregate fair value computed as of the grant date of the options awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standard Codification, or ASC, Topic 718. See note 10 to our consolidated financial statements appearing at the end of this prospectus for assumptions underlying the valuation of equity awards.

(3) Consists of $10,200 that we matched pursuant to our 401(k) plan and $768 in life insurance premiums.

Narrative to summary compensation table

Base salary. In 2013, we paid base salaries of $352,000 to Dr. Fetzer, $295,000 to Mr. Guiffre and $303,000 to Dr. Garmey. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all of our employees, including our named executive officers. None of our named executive officers are party to an employment agreement, or other agreement or arrangement, that provides for automatic or scheduled increases in base salary. In December 2013, our compensation committee approved 2014 base salaries of $310,000 for Mr. Guiffre and $309,000 for Dr. Garmey. In January 2014, our board of directors, upon the recommendation of our compensation committee, approved a 2014 base salary of $366,080 for Dr. Fetzer.

Annual bonus. Our board of directors may, in its discretion, award bonuses to our named executive officers from time to time. We typically establish annual bonus targets based on a set of specified corporate goals for our named executive officers and conduct an annual performance review to determine the attainment of such goals. Our management may propose bonus awards to the compensation committee of the board or the board primarily based on such review process. Our compensation committee makes the final determination of the eligibility requirements for and the amount of the bonus awards paid to our executive officers other than our Chief Executive Officer, and our board of directors makes the final determination of the eligibility requirements for and the amount of the bonus awards paid to our Chief Executive Officer. With respect to 2013, we awarded bonuses, payable in March 2014, of $176,000 to Dr. Fetzer, $73,750 to Mr. Guiffre and $75,750 to Dr. Garmey, in each case based on our achievement of company goals, with such amount representing 100% of each such officer's bonus target.

Equity incentives. Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. Accordingly, our compensation committee and board of directors periodically review the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options. Prior to this offering, our executives were eligible to participate in the 2007 stock incentive plan, as amended, or the 2007 Plan. During 2013, all stock options were granted pursuant to the 2007 Plan. Following the closing of this offering, our employees and executives will be eligible to receive stock options and other stock-based awards pursuant to the 2014 stock incentive plan, or the 2014 Plan.

We use stock options to compensate our executive officers in the form of initial grants in connection with the commencement of employment and also at various times, often but not necessarily annually, if we have performed as expected or better than expected. Prior to this offering, the award of stock options to our executive officers, other than our Chief Executive Officer, has been made by our board or compensation committee, and the award of stock options to our Chief Executive Officer has been made by our board. None of our executive officers is currently party to an employment agreement that provides for automatic award of stock options. We have granted stock options to our executive officers with both time-based and performance-based vesting. The options that we have granted to our executive officers with time-based vesting typically become exercisable as to 25% of the shares underlying the option on the first anniversary of the grant date, and as to an additional 1/48th of the shares underlying the option monthly thereafter. Going forward, we expect annual and other grants made to existing executive officers and employees will vest monthly as to 1/48th of the shares underlying the option. The options that we have granted to date to our executive officers with performance-based vesting become exercisable upon the occurrence of specified business transactions or other specified milestones. Vesting and exercise rights cease shortly after termination of employment except in the case of death or disability and, in the case of Dr. Fetzer, in certain circumstances upon a change in control. Prior to the exercise of an option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents.

We have historically granted stock options with exercise prices that are equal to the fair market value of our common stock on the date of grant as determined by our board of directors, based on a number of objective and subjective factors. The exercise price of all stock options granted after the closing of this offering will be equal to the fair market value of shares of our common stock on the date of grant, which will be determined by reference to the closing market price of our common stock on the date of grant.

In January 2014, our board of directors granted an option to purchase 27,572 shares to Dr. Fetzer, an option to purchase 17,922 shares to Mr. Guiffre and an option to purchase 13,786 shares to Dr. Garmey. These options have an exercise price of $10.59 per share and vest monthly as to 1/48th of the shares underlying the option over four years following the grant date.

2013 Outstanding Option Awards at Fiscal-Year End

The following table sets forth information concerning outstanding option awards for each of our named executive officers at December 31, 2013:

	Option Awards			
Name	**Number of Securities Underlying Unexercised Options (#) Exercisable**	**Number of Securities Underlying Unexercised Options (#) Unexercisable**	**Option Exercise Price ($)**	**Option Expiration Date**
Oliver S. Fetzer, Ph.D.	95,981	—	5.95	4/7/2019
	17,233	—	3.34	12/3/2019
	8,313	—	3.34	2/2/2020
	99,161	33,054(1)	3.34	1/27/2021
	23,092	23,091(2)	3.77	1/24/2022
	8,382	81,202(3)	3.92	12/26/2022
	0	53,488(4)	3.92	2/6/2023
Christopher D.T. Guiffre, J.D.	25,763	28,003(5)	3.77	1/24/2022
	0	51,698(6)	3.77	1/24/2022
	2,309	6,927(7)	3.92	12/18/2022
	0	9,236(8)	3.92	12/18/2022
Edward Garmey, M.D.	22,259	12,206(9)	3.34	6/8/2021
	9,650	9,650(10)	3.77	1/24/2022
	3,157	9,471(11)	3.92	12/18/2022

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(1) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through December 31, 2014.

(2) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through December 31, 2015.

(3) This option vests as follows: (i) 33,532 of the underlying shares shall vest as to 25% of such shares on December 31, 2013, with the remaining shares scheduled to vest in approximately equal monthly installments through December 31, 2016; (ii) an additional 17,159 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share; (iii) an additional 17,159 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share and (iv) an additional 21,734 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share.

(4) This option vests as follows: (i) 16,374 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share; (ii) an additional 16,374 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share and (iii) an additional 20,740 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share.

(5) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through January 17, 2016.

(6) This option vests as follows: (i) 27,572 of the underlying shares shall vest in 24 approximately equal monthly installments, commencing upon the closing of a transformative business development transaction, as determined by our board of directors and (ii) the remaining 24,126 shares shall vest upon the occurrence of a change in control event meeting certain objective criteria.

(7) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through December 31, 2016.

(8) This option vests as follows: (i) 4,988 of the underlying shares shall vest in 24 approximately equal monthly installments, commencing upon the closing of a transformative business development transaction, as determined by our board of directors and (ii) the remaining 4,248 shares shall vest upon the occurrence of a change in control event meeting certain objective criteria, provided that if the closing of such change of control event occurs on or prior to January 1, 2015 then, upon such closing, all of the shares underlying this option shall vest in full.

(9) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through May 2, 2015.

(10) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through December 31, 2015.

(11) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through December 31, 2016.

Employment Agreements

Agreements with Dr. Fetzer

In April 2009, we entered into an employment agreement with Dr. Fetzer in connection with the commencement of his employment with us. This agreement provides that Dr. Fetzer is employed at will, and either we or Dr. Fetzer may terminate the employment relationship for any reason, at any time, with or without notice.

Pursuant to the agreement, Dr. Fetzer is eligible to receive a performance-based annual cash bonus, which is based upon quantitative and qualitative performance objectives that will be mutually agreed between our board of directors and Dr. Fetzer, and which will be determined by our board of directors in its sole discretion. Dr. Fetzer’s target annual bonus is 50% of his base salary for the applicable fiscal year.

If we terminate Dr. Fetzer’s employment without cause or if Dr. Fetzer terminates his employment with us for good reason, each as defined in the employment agreement, other than in connection with a change in control, as defined in the employment agreement, upon execution and effectiveness of a release of claims, we are obligated to pay Dr. Fetzer a lump sum amount equal to his then-current base salary for nine months plus an amount equal to three-fourths of the amount of the last bonus paid by us to Dr. Fetzer and, to the extent allowed by applicable law and the applicable plan documents, to continue to provide Dr. Fetzer and certain of his dependents with group health insurance for a period of nine months.

If we terminate Dr. Fetzer’s employment without cause or if Dr. Fetzer terminates his employment with us for good reason, in each case within 12 months following a change of control, upon execution and effectiveness of a release of claims, we are obligated to pay Dr. Fetzer a lump sum amount equal to his base salary for twelve months plus an amount equal to the amount of the last bonus paid by us to Dr. Fetzer, to continue to provide Dr. Fetzer and certain of his dependents with group health insurance for a period of 12 months and to accelerate in full the vesting of Dr. Fetzer’s outstanding equity awards that are subject to time-based vesting.

In addition, with respect to the options to purchase 109,541 shares of our common stock subject to performance-based vesting that were granted to Dr. Fetzer in December 2012 and February 2013, he will be entitled to certain cash payments following a change in control to the extent such options are not fully vested at the time of the change in control and future cash consideration is paid in connection with the transaction, which payments would have resulted in more shares vesting pursuant to the option agreement if they had they been paid at the time of the closing of the change in control.

Offer Letters with Dr. Garmey and Mr. Guiffre

In April 2011 and January 2012, we entered into employment offer letters with Dr. Garmey and Mr. Guiffre, respectively, pursuant to which they are employed at will, and either we or they may terminate the respective employment relationship at any time for any reason. The offer letters establish each of Dr. Garmey's and Mr. Guiffre's title, initial compensation arrangement, eligibility for benefits made available to employees generally and, subject to certain criteria determined by our compensation committee, eligibility for a discretionary performance-based bonus with a target of 25% of their respective annual base salary.

Change in Control Severance Plan

We have established a Change in Control Severance Plan, or the Severance Plan, which sets forth the conditions under which certain of our employees with a job title of vice president or above will receive severance benefits if we terminate their employment under specified circumstances, as described below. We believe that change in control benefits are important for attracting and retaining senior level talent and help to ensure that our senior level employees can remain focused during periods of uncertainty.

The Severance Plan covers our employees with a job title of vice president or above, other than those employees (i) who are party to an employment, retention or other agreement with us that provides for severance benefits, (ii) whose employment is terminated for cause, as defined in the Severance Plan, (iii) who retire, terminate their employment as a result of an inability to perform their duties due to physical or mental disability or die, (iv) who voluntarily terminate their employment, other than for good reason, as defined in the Severance Plan, (v) who are employed for a specified period of time in accordance with the terms of a written employment agreement or (vi) who accept employment with an acquirer of any of our businesses, operations or assets or who refuse an offer of such employment in a position providing comparable responsibilities or compensation. We sometimes refer to the employees who are covered by the Severance Plan as the covered employees.

Under the Severance Plan, if, within the one-year period following a change in control, as defined in the Severance Plan, we terminate the employment of a covered employee without cause, as defined in the Severance Plan, or the employee resigns for good reason, as defined in the Severance Plan, such employee is entitled to receive the following cash severance pay and other severance benefits. Under the Severance Plan, covered employees are entitled to receive a lump sum payment equal to six months of the employee's then-current monthly base salary. Covered employees at the level of senior vice president or higher are also entitled to receive one additional month for each year of service, up to a maximum of nine additional months. In addition to the cash severance pay, under the Severance Plan covered employees are entitled to:

- full acceleration of the vesting of unvested equity awards, other than awards with vesting based on performance or the achievement of milestones;
- payment of any bonus amount for the prior year that was approved but not yet paid at the time of termination, such amount to be paid in a manner consistent with payments to other similarly situated employees and consistent with the requirements of Section 409A of the Internal Revenue Code; and
- contributions to the cost of Consolidated Omnibus Budget Reconciliation Act, or COBRA, coverage on behalf of the employee and any applicable dependents, if the employee elects such coverage and for no longer than the period for which such employee is entitled to cash severance pay as described above.

Cash severance pay and other severance benefits under the Severance Plan are conditioned on the covered employee's execution and delivery of a release of claims against us and the employee's compliance with any applicable noncompetition, nonsolicitation or other obligations to us. If a covered employee fails to comply with the terms of such release and obligations, we may recoup from such employee the applicable cash severance pay, COBRA contributions or the value of equity award acceleration provided to the employee under the Severance Plan.

The Severance Plan is administered by our board of directors or a qualified administrator appointed by the board. Our board of directors may amend, modify or terminate the Severance Plan at any time in its sole discretion, provided that (i) any such amendment, modification or termination made prior to a change in control that adversely affects the rights of any covered employee shall be approved by a majority of our board of directors, including our Chief Executive Officer, (ii) no such amendment, modification or termination may affect the rights of a covered employee then receiving payments or benefits under the Severance Plan without the consent of such person, and (iii) neither we, our board of directors, any of our successors, nor the plan administrator may amend, modify or terminate the Severance Plan for one year following a change in control. Our board of directors intends to review the Severance Plan at least annually.

Other Agreements

We have entered into non-disclosure, non-competition and assignment of intellectual property agreements with each of our executive officers. Under the non-disclosure, non-competition and assignment of intellectual property agreements, each executive officer has agreed (1) to protect our confidential and proprietary information, (2) to assign to us related intellectual property that is developed during such executive officer’s employment and that relates to our business or research and development or from the use of our property, premises or confidential information, (3) not to compete with us during his or her employment and for a period of one year after the termination of his or her employment and (4) not to solicit our employees or customers during his or her employment and for a period of one year after the termination of his or her employment.

Stock Option and Other Compensation Plans

2007 Stock Incentive Plan

The 2007 Plan was first adopted by our board of directors in February 2007 and first approved by our stockholders in March 2007 and was amended in May 2007, April 2009, September 2009, March 2010, November 2010, October 2011, December 2011, November 2012, January 2013, February 2013 and January 2014 to increase the number of shares available for issuance under the plan. The 2007 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock, restricted stock units and other stock-based awards. Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2007 Plan. However, incentive stock options may only be granted to our employees.

Our board of directors administers the 2007 Plan. Pursuant to the terms of the 2007 Plan, our board of directors selects the recipients of awards and determines:

- the number of shares of our common stock covered by options;
- the type of options to be granted;
- the terms, conditions and limitations applicable to the exercise of options;
- the duration of options;
- the exercise price of options; and
- the number of shares of our common stock subject to, and the terms and conditions of, any awards of restricted stock, restricted stock units, and other stock-based awards, including conditions for vesting and repurchase (or forfeiture) and the issue price or purchase price, if any.

To the extent permitted by applicable law, our board of directors may delegate its powers under the 2007 Plan to one or more committees or subcommittees of our board.

As of February 28, 2014, (i) there were 1,275,212 shares of our common stock reserved for issuance under the 2007 Plan, subject to adjustment as provided below in connection with changes in capitalization and (ii) there were outstanding options to purchase an aggregate of 1,215,315 shares of common stock at a weighted-average exercise price of $4.84 per share. Upon the closing of this offering, we will grant no further stock options or other awards under the 2007 Plan, but awards outstanding under the 2007 Plan may extend beyond that date. However, any shares of common stock reserved for issuance under the 2007 Plan that remain available for grant immediately prior to the closing of this offering and any shares of common stock subject to awards under the 2007 Plan that expire, terminate, or are otherwise surrendered, canceled, forfeited or repurchased at their original issuance price pursuant to a contractual repurchase right shall be available for issuance under the 2014 Stock Incentive Plan (subject, in the case of incentive stock options, to any limitations of the Internal Revenue Code).

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend:

- the number and class of securities available under the 2007 Plan;
- the number and class of securities and exercise price per share of each outstanding option under the 2007 Plan;
- the number of shares subject to and the repurchase price per share subject to each outstanding restricted stock award under the 2007 Plan; and/or
- the terms of each other outstanding award under the 2007 Plan

shall be equitably adjusted by us (or substitute awards may be made, if applicable) in a manner determined by our board of directors.

Upon a reorganization event, as defined in the 2007 Plan, our board of directors may, in the case of awards under the 2007 Plan, take one or more of the following actions as to all or any, or any portion of, outstanding awards, other than restricted stock awards:

- provide that each outstanding award will be assumed or a substantially similar award will be substituted by the acquiring or succeeding corporation (or an affiliate thereof);
- provide, upon notice to the participant, that unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised within a specified period of time following the date of such notice;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to such awards will lapse, in full or in part, at or immediately prior to such reorganization event;
- in the event of a reorganization event pursuant to which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to a participant equal to the excess, if any, of (i) the acquisition price times the number of shares of our common stock subject to such participant’s outstanding awards (to the extent then exercisable at prices not in excess of the acquisition price), over (ii) the aggregate exercise price of all such outstanding awards and any applicable tax withholdings, in exchange for the termination of such awards;
- provide that in the event of a liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated under the 2007 Plan to treat all awards, or all awards of the same type, identically.

Upon a reorganization event, as defined in the 2007 Plan, other than a liquidation or dissolution, the repurchase and other rights we may have under each outstanding restricted stock award under the 2007 Plan shall inure to the benefit of our successor and shall, unless our board of directors determines otherwise, apply to the cash, securities or other property which our common stock was converted into or exchanged for pursuant to such reorganization event in the same manner and to the same extent as they applied to the common stock subject to such restricted stock award. Upon a reorganization event involving a liquidation or dissolution, except to the extent specifically provided to the contrary in the instrument evidencing any restricted stock award under the 2007 Plan or any other agreement between a participant and us, all restrictions and conditions on all restricted stock awards then outstanding shall automatically be deemed terminated or satisfied.

Our board of directors may at any time provide that any award under the 2007 Plan shall become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in full or in part. Our board of directors may amend, modify or terminate any outstanding award under the 2007 Plan, including but not limited to, substituting another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option to a nonstatutory stock option, subject in certain cases to the participant's consent. Our board of directors may amend, suspend or terminate the 2007 Plan or any portion thereof at any time, subject to any stockholder approval requirements under the Internal Revenue Code with respect to incentive stock options. Unless otherwise specified in the amendment, any amendment to the 2007 Plan will apply to, and be binding on the holders of, all awards outstanding under the 2007 Plan at the time the amendment is adopted, provided that our board of directors determines that such amendment does not materially and adversely affect the rights of participants under the 2007 Plan.

2014 Stock Incentive Plan

In March 2014, our board of directors adopted and our stockholders approved the 2014 Stock Incentive Plan, or 2014 Plan, which will become effective upon the closing of this offering. 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. Upon effectiveness of the 2014 Plan, the number of shares of our common stock that will be reserved for issuance under the 2014 Plan will equal the sum of (1) 2,400,000 shares plus (2) the number of shares (up to 1,221,651 shares) equal to the sum of the number of shares of our common stock then available for grant under the 2007 Plan and the number of shares of our common stock subject to outstanding awards under the 2007 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right (subject, in the case of incentive stock options, to any limitations of the Internal Revenue Code) plus (3) an annual increase to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2015 and continuing until, and including, the fiscal year ending December 31, 2024, equal to the least of (A) 1,000,000 shares of our common stock, (B) 4% of the number of shares of our common stock outstanding on the first day of the fiscal year, and (C) an amount determined by our board of directors.

Our employees, officers, directors, consultants and advisors will be eligible to receive awards under the 2014 Plan; however, incentive stock options may only be granted to our employees.

The 2014 Plan will be administered by our board of directors. Pursuant to the terms of the 2014 Plan, our board of directors will select the recipients of awards and determine:

- the number of shares of common stock covered by options and the conditions and limitations applicable to the exercise of options;
- the type of options to be granted;
- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant;
- the duration of options, which may not be in excess of ten years; and
- the number of shares of common stock subject to any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including the issue price or purchase price (if any) and conditions for vesting and repurchase (or

forfeiture), provided that the measurement price for stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of stock appreciation rights may not be in excess of ten years.

To the extent permitted by applicable law, our board of directors may delegate its powers under the 2014 Plan to one or more committees or subcommittees of our board or to one or more of our officers. If our board of directors delegates authority to an officer to grant awards under the 2014 Plan, the officer will have the power to make awards to all of our employees, except executive officers. Our board of directors will fix the terms of the awards to be granted by such officer, including the exercise price of such awards (which may include a formula by which the exercise price will be determined), and the maximum number of shares subject to awards that such officer may make.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, our board of directors is required by the 2014 Plan to make equitable adjustments, in a manner determined by our board, to:

- the number and class of securities available and the share counting rules under the 2014 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share-related provisions and purchase price, if any, of any outstanding other stock-based award.

Upon a reorganization event, as defined in the 2014 Plan, our board of directors, may, in its sole discretion, take any one or more of the following actions pursuant to the 2014 Plan, as to some or all outstanding awards, other than restricted stock:

- provide that all outstanding awards will be assumed, or substituted equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to a participant, provide that the participant’s unvested and/or unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of such notice;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon the reorganization event;
- in the event of a reorganization event pursuant to which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (i) the number of shares of common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (ii) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such awards;
- provide that, in connection with a liquidation or dissolution, awards convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); and/or
- any combination of the foregoing.

Our board of directors is not obligated under the 2014 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock unit awards, no assumption or substitution will be permitted and the restricted stock unit awards will instead be settled in accordance with the terms of the applicable restricted stock unit agreement, and in certain circumstances, any unvested restricted stock unit awards will be terminated immediately prior to the consummation of the reorganization event without any payment in exchange therefor.

Upon the occurrence of a reorganization event other than a liquidation or dissolution, the repurchase and other rights under each outstanding restricted stock award will continue for the benefit of the successor company and will, unless our board of directors may otherwise determine, apply to the cash, securities or other property into which our common stock is converted pursuant to the reorganization event in the same manner and to the same extent as they applied to such restricted stock. Upon the occurrence of a reorganization event involving a liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award or any other agreement between a participant and us.

At any time, our board of directors may provide that any award under the 2014 Plan shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

Except with respect to certain actions requiring stockholder approval under the Internal Revenue Code or the rules of the NASDAQ Stock Market, our board of directors may amend, modify or terminate any outstanding award under the 2014 Plan, including but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option into a nonstatutory stock option, subject to certain participant consent requirements. Unless our stockholders approve such action, the 2014 Plan provides that the we may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

- amend any outstanding stock option or stock appreciation right granted under the 2014 Plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding option or stock appreciation right (whether or not granted under the 2014 Plan) and grant in substitution therefor new awards under the 2014 Plan (other than substitute awards permitted in connection with a merger or consolidation of an entity with us or our acquisition of property or stock of another entity) covering the same or a different number of shares of our common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;
- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock; or
- take any other action that constitutes a “repricing” within the meaning of the rules of the NASDAQ Stock Market.

No award may be granted under the 2014 Plan after March 26, 2024, but awards previously granted may extend beyond that date. Our board of directors may amend, suspend or terminate the 2014 Plan or any portion thereof at any time, except that stockholder approval will be required to comply with the Internal Revenue Code or stock market requirements.

2014 Employee Stock Purchase Plan

In March 2014, our board of directors adopted and our stockholders approved the 2014 employee stock purchase plan, or the 2014 ESPP, which will become effective upon the closing of this offering. The 2014 ESPP will be administered by our board of directors or by a committee appointed by our board of directors. The 2014 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate 500,000 of shares of our common stock. The number of shares of our common stock reserved for issuance under the 2014 ESPP will automatically increase on the first day of each fiscal year, commencing on January 1, 2015 and ending on January 1, 2024, in an amount equal to the least of (i) 600,000 shares of our common stock, (ii) 1% of the total number of shares of our common stock outstanding on the first day of the applicable year, and (iii) an amount determined by our board of directors.

All of our employees or employees of any designated subsidiary, as defined in the 2014 ESPP, are eligible to participate in the 2014 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least 30 days prior to enrolling in the 2014 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2014 ESPP.

No employee may purchase shares of our common stock under the 2014 ESPP and any of our other employee stock purchase plans in excess of $25,000 of the fair market value of our common stock (as of the date of the option grant) in any calendar year. In addition, no employee may purchase shares of our common stock under the 2014 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2014 ESPP beginning at such time as our board of directors may determine. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors may, at its discretion, choose a different period of not more than 12 months for offerings.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2014 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2014 ESPP, the purchase price shall be determined by our board of directors for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee who is not a participant on the last day of the offering period is not entitled to purchase shares under the 2014 ESPP, and the employee’s accumulated payroll deductions will be refunded. An employee’s rights under the 2014 ESPP terminate upon voluntary withdrawal from an offering under the 2014 ESPP at any time, or when the employee ceases employment for any reason.

We will be required to make equitable adjustments to the number and class of securities available under the 2014 ESPP, the share limitations under the 2014 ESPP, and the purchase price for an offering period under the

2014 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event, as defined in the 2014 ESPP, our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2014 ESPP on such terms as our board or committee determines:

- provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our board or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the acquisition price is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2014 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or
- provide that, in connection with our liquidation or dissolution, options shall convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2014 ESPP or any portion thereof. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Internal Revenue Code. Further, our board of directors may not make any amendment that would cause the 2014 ESPP to fail to comply with Section 423 of the Internal Revenue Code. The 2014 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

401(k) retirement plan

We maintain a defined contribution employee retirement plan for our employees. Our 401(k) plan is intended to qualify as a tax-qualified plan under Section 401 of the Internal Revenue Code so that contributions to our 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan. Our 401(k) plan provides that each participant may contribute up to 100% of his or her pre-tax compensation, up to a statutory limit, which was $17,000 for 2012 and $17,500 for 2013. Participants who are at least 50 years old can also make "catch-up" contributions, which in 2012 and 2013 could be up to an additional $5,500 above the statutory limit. Under our 401(k) plan, each employee is fully vested in his or her deferred salary contributions. Employee contributions are held and invested by the plan's trustee, subject to participants' ability to give investment directions by following certain procedures. We match participant contributions up to 4% of a participant's annual compensation, subject to statutory limits.

2013 Director Compensation

The following table sets forth information regarding compensation earned by our non-employee directors during 2013.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)	Total ($)
Alan L. Crane(2)	—	97,681	97,681
Paul A. Friedman, M.D.(3)	—	—	—
Steven E. Hall, Ph.D.	—	—	—
William T. McKee(3)	—	—	—
William H. Rastetter, Ph.D.(3)	—	—	—
Ram Sasisekharan, Ph.D.	12,500(4)	—	12,500
Robert I. Tepper, M.D.	—	—	—

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(1) The amount reported in the "Option Awards" column reflect the aggregate fair value computed as of the grant date of the options awarded during the year computed in accordance with the provisions of FASB ASC, Topic 718. See note 10 to our consolidated financial statements appearing at the end of this prospectus for assumptions underlying the valuation of equity awards. Including these options, as of December 31, 2013:

- Mr. Crane held stock options to purchase 52,998 shares of common stock, which were vested with respect to 17,233 shares in the aggregate; and
- Dr. Tepper held stock options to purchase 3,447 shares of common stock, which were vested with respect to 1,723 shares in the aggregate.

(2) The option granted to Mr. Crane in 2013 was granted in recognition of his services to us other than in his role as a director. This option vests as follows: (i) 11,922 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share; (ii) an additional 11,922 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share and (iii) an additional 11,921 of the shares shall vest either upon the occurrence of a change in control event meeting certain objective criteria or our stock reaching a specified average price per share. In addition, with respect to this option, Mr. Crane will be entitled to certain cash payments following a change in control to the extent such option is not fully vested at the time of the change in control and future cash consideration is paid in connection with the transaction, which payments would have resulted in more shares vesting pursuant to the option agreement if they had they been paid at the time of the closing of the change in control.

(3) Each of Dr. Friedman, Mr. McKee and Dr. Rastetter joined our board of directors in January 2014.

(4) The payments made to Dr. Sasisekharan were made in exchange for services Dr. Sasisekharan provided in 2013 pursuant to a consulting agreement with us.

Prior to this offering, we did not have a formal non-employee director compensation policy. We did not compensate any non-employee director for his service as a director in 2013. We have historically reimbursed our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings. Dr. Fetzer, one of our directors who also serves as our President and Chief Executive Officer, does not receive any additional compensation for his service as a director. The compensation that we pay to our President and Chief Executive Officer is discussed in the "Executive Compensation" section of this prospectus.

In January 2014, in connection with their election to our board, we granted each of Dr. Friedman, Mr. McKee and Dr. Rastetter an option to purchase 13,786 shares of our common stock. The options each have an exercise price of $10.59 and vest in three equal annual installments beginning on the first anniversary of such director's election.

Director compensation policy following this offering

Our board has established the following compensation policy for non-employee directors, effective upon the closing of this offering:

- each non-employee director will receive, on an annual basis, a cash retainer of $30,000;

- each non-employee director who has then served on our board of directors for at least six months will receive, on the date of the first board meeting held after each year’s annual meeting of stockholders, an option to purchase 8,000 shares of our common stock, which shall vest in full on the earlier of the first anniversary of the date of grant or immediately prior to the first annual meeting of stockholders occurring after the date of grant;
- the chairman of our board of directors will receive an additional cash retainer of $30,000;
- each non-employee director who serves on the audit committee will receive a cash retainer of $7,500 per year ($15,000 for the chair);
- each non-employee director who serves on the compensation committee will receive a cash retainer of $5,000 per year ($10,000 for the chair);
- each non-employee director who serves on the nominating and corporate governance committee will receive a cash retainer of $3,500 ($7,000 for the chair); and
- each non-employee director elected to the board following the closing of this offering will receive a one-time award of an option to purchase 15,000 shares of our common stock, which option shall vest in three equal annual installments.

In addition, we will continue to reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending board of director and committee meetings.

Limitation of Liability and Indemnification

As permitted by Delaware law, we have adopted provisions in our certificate of incorporation, which will be effective as of the closing date of this offering, that limit or eliminate the personal liability of our directors. Our certificate of incorporation limits the liability of directors to the maximum extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for breaches of their fiduciary duties as directors, except liability for:

- any breach of the director’s duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock repurchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations do not apply to liabilities arising under federal securities laws and do not affect the availability of equitable remedies, including injunctive relief or rescission. If Delaware law is amended to authorize the further elimination or limiting of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law as so amended.

- we will indemnify our directors and officers to the fullest extent permitted by law;
- we may indemnify our other employees and other agents to the same extent that we indemnify our officers and directors, unless otherwise determined by our board of directors; and
- we will advance expenses to our directors and officers in connection with legal proceedings in connection with a legal proceeding to the fullest extent permitted by law.

The indemnification provisions contained in our certificate of incorporation that will be effective as of the closing date of this offering are not exclusive. In addition, we have entered into indemnification agreements with our directors and executive officers. These indemnification agreements require us, among other things, to indemnify each such director and executive officer for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or executive officers.

We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and officers. Insofar as indemnification for liabilities arising under the Securities Act of 1933, which we refer to as the Securities Act, may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we understand that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

In addition, we maintain standard policies of insurance under which coverage is provided to our directors and officers against losses arising from claims made by reason of breach of duty or other wrongful act, and to us with respect to payments which may be made by us to such directors and officers pursuant to the above indemnification provisions or otherwise as a matter of law.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

Since January 1, 2011, we have engaged in the following transactions with our directors and executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and 5% stockholders. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties.

Series C Preferred Stock Financing

In June 2011, we issued and sold an aggregate of 10,135,128 shares of our Series C convertible preferred stock at a price of $0.74 per share for an aggregate purchase price of approximately $7.5 million. The following table sets forth the aggregate number of shares of our Series C convertible preferred stock that we issued to our officers, directors and 5% stockholders and their respective affiliates in these transactions.

Purchaser	Shares of Series C Convertible Preferred Stock	Purchase Price ($)
Entities affiliated with Polaris Partners(1)	2,971,846	2,199,166
Entities affiliated with Venrock(2)	1,857,545	1,374,583
Entities affiliated with Lux Capital(3)	836,104	618,717
Lilly Ventures Fund I LLC(4)	4,222,973	3,125,000
William H. Rastetter(5)	37,173	27,508

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(1) Consists of (a) 687,062 shares of Series C convertible preferred stock purchased by Polaris Venture Partners V, L.P.; (b) 13,390 shares of Series C convertible preferred stock purchased by Polaris Venture Partners Entrepreneurs' Fund V, L.P.; (c) 4,706 shares of Series C convertible preferred stock purchased by Polaris Venture Partners Founders' Fund V, L.P.; (d) 6,870 shares of Series C convertible preferred stock purchased by Polaris Venture Partners Special Founders' Fund V, L.P.; (e) 2,218,233 shares of Series C convertible preferred stock purchased by Polaris Venture Partners IV, L.P. and (f) 41,585 shares of Series C convertible preferred stock purchased by Polaris Venture Partners Entrepreneurs' Fund IV, L.P. Alan Crane, a member of our board of directors, is a general partner of Polaris Venture Partners, an affiliate of Polaris Venture Partners V, L.P., Polaris Venture Partners Entrepreneurs' Fund V, L.P., Polaris Venture Partners Founders' Fund V, L.P., Polaris Venture Partners Special Founders' Fund V, L.P., Polaris Venture Partners IV, L.P. and Polaris Venture Partners Entrepreneurs' Fund IV, L.P. (collectively, the "Polaris Funds").

(2) Consists of (a) 1,676,063 shares of Series C convertible preferred stock purchased by Venrock Associates V, L.P.; (b) 142,201 shares of Series C convertible preferred stock purchased by Venrock Partners V, L.P. and (c) 39,380 shares of Series C convertible preferred stock purchased by Venrock Entrepreneurs Fund V, L.P.

(3) Consists of (a) 688,969 shares of Series C convertible preferred stock purchased by Lux Ventures II, L.P.; (b) 28,892 shares of Series C convertible preferred stock purchased by Lux Ventures II Sidecar, L.P. and (c) 118,243 shares of Series C convertible preferred stock purchased by Lux Ventures II Partners Fund I LLC.

(4) Steven E. Hall, a member of our board of directors, is a venture partner of Lilly Ventures Fund I LLC.

(5) Consists of shares held by William H. Rastetter and Marisa G. Rastetter as community property. Dr. Rastetter is a member of our board of directors.

Series D Convertible Preferred Stock Financing

In December 2011, we issued and sold an aggregate of 18,072,287 shares of our Series D convertible preferred stock at a price of $0.83 per share for an aggregate purchase price of approximately $15.0 million. In November 2012, we issued and sold an aggregate of 15,662,650 shares of our Series D convertible preferred stock at a price of $0.83 per share for an aggregate purchase price of approximately $13.0 million.

The following table sets forth the aggregate number of shares of our Series D convertible preferred stock that we issued to our officers, directors and 5% stockholders and their respective affiliates.

Purchaser	Shares of Series D Convertible Preferred Stock	Purchase Price ($)
Entities affiliated with Polaris Partners(1)	8,598,139	7,136,455
Entities affiliated with Venrock(2)	5,500,704	4,565,584
Entities affiliated with Lux Capital(3)	2,488,436	2,065,402
Lilly Ventures Fund 1 LLC(4)	4,340,831	3,602,890
CVF, LLC	12,048,192	10,000,000
William H. Rastetter(5)	110,107	91,389

(1) Consists of (a) 5,320,189 shares of Series D convertible preferred stock purchased by Polaris Venture Partners V, L.P.; (b) 103,691 shares of Series D convertible preferred stock purchased by Polaris Venture Partners Entrepreneurs’ Fund V, L.P.; (c) 36,444 shares of Series D convertible preferred stock purchased by Polaris Venture Partners Founders’ Fund V, L.P.; (d) 53,200 shares of Series D convertible preferred stock purchased by Polaris Venture Partners Special Founders’ Fund V, L.P.; (e) 3,027,852 shares of Series D convertible preferred stock purchased by Polaris Venture Partners IV, L.P. and (f) 56,763 shares of Series D convertible preferred stock purchased by Polaris Venture Partners Entrepreneurs’ Fund IV, L.P. Alan Crane, a member of our board of directors, is a general partner of Polaris Venture Partners, an affiliate of the Polaris Funds.

(2) Consists of (a) 4,963,287 shares of Series D convertible preferred stock purchased by Venrock Associates V, L.P.; (b) 420,803 shares of Series D convertible preferred stock purchased by Venrock Partners V, L.P. and (c) 116,614 shares of Series D convertible preferred stock purchased by Venrock Entrepreneurs Fund V, L.P.

(3) Consists of (a) 2,270,840 shares of Series D convertible preferred stock purchased by Lux Ventures II, L.P.; (b) 95,229 shares of Series D convertible preferred stock purchased by Lux Ventures II Sidecar, L.P. and (c) 122,367 shares of Series D convertible preferred stock purchased by Lux Ventures II Partners Fund I LLC.

(4) Steven E. Hall, a member of our board of directors, is a venture partner of Lilly Ventures Fund I LLC.

(5) Consists of shares held by William H. Rastetter and Marisa G. Rastetter as community property. Dr. Rastetter is a member of our board of directors.

Agreement with Arsia Therapeutics, Inc.

In April 2013, we entered into a laboratory, equipment sharing, services and license agreement with Arsia Therapeutics, Inc. Arsia Therapeutics provided us with a notice of termination and the arrangement will terminate in April of 2014. Pursuant to this agreement, Arsia Therapeutics paid us $84,000 during 2013 and, during 2014, will pay us approximately $50,000. In addition, we may enter into an additional agreement with Arsia Therapeutics, pursuant to which we will sell it an excess piece of equipment. Alan Crane, who is one of our directors, is the President and a director of Arsia Therapeutics.

Bridge Financing

In August 2013, we issued and sold 7% convertible promissory notes in an aggregate principal amount of $8,823,903. We refer to these notes as our 2013 convertible notes. The following table sets forth the principal amount of our 2013 convertible notes that we issued to our directors, officers and 5% stockholders and their respective affiliates.

Name	Aggregate Principal Amount of 2013 Convertible Notes ($)	Number of Shares of Common Stock Issuable upon Conversion of 2013 Convertible Notes(1)
CVF, LLC	3,000,000	261,651
Entities affiliated with Polaris Partners(2)	2,577,902	224,837
Entities affiliated with Venrock(3)	1,655,363	144,376
Lilly Ventures Fund I LLC(4)	1,285,556	112,122
Entities affiliated with Lux Capital(5)	250,000	21,804
William H. Rastetter(6)	33,135	2,890

(1) The number of shares of common stock issuable upon conversion of our 2013 convertible notes is determined based on an assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and assuming this offering closes on April 15, 2014.

(2) Consists of 2013 convertible notes issued and sold to (a) Polaris Venture Partners V, L.P. in a principal amount of $2,487,507; (b) Polaris Venture Partners Entrepreneurs' Fund V, L.P. in a principal amount of $48,481; (c) Polaris Venture Partners Founders' Fund V, L.P. in a principal amount of $17,039 and (d) Polaris Venture Partners Special Founders' Fund V, L.P. in a principal amount of $24,875. Alan Crane, a member of our board of directors, is a general partner of Polaris Venture Partners, an affiliate of Polaris Venture Partners V, L.P., Polaris Venture Partners Entrepreneurs' Fund V, L.P., Polaris Venture Partners Founders' Fund V, L.P. and Polaris Venture Partners Special Founders' Fund V, L.P.

(3) Consists of 2013 convertible notes issued and sold to (a) Venrock Associates V, L.P. in a principal amount of $1,493,634; (b) Venrock Partners V, L.P. in a principal amount of $126,635 and (c) Venrock Entrepreneurs Fund V, L.P. in a principal amount of $35,094.

(4) Steven E. Hall, a member of our board of directors, is a venture partner of Lilly Ventures Fund I LLC.

(5) Consists of 2013 convertible notes issued and sold to (a) Lux Ventures II, L.P. in a principal amount of $228,139; (b) Lux Ventures II Sidecar, L.P. in a principal amount of $9,567 and (c) Lux Ventures II Partners Fund I LLC in a principal amount of $12,294.

(6) Consists of 2013 convertible notes issued and sold to William H. Rastetter and Marisa G. Rastetter as community property. Dr. Rastetter is a member of our board of directors.

In February 2014, we issued and sold 7% convertible promissory notes in an aggregate principal amount of $6,000,000. The following table sets forth the principal amount of the convertible promissory notes that we issued to our directors, officers and 5% stockholders and their respective affiliates.

Name	Aggregate Principal Amount of 2014 Convertible Notes ($)	Number of Shares of Common Stock Issuable upon Conversion of 2014 Convertible Notes(1)
CVF, LLC	819,319	89,113
Entities affiliated with Polaris Partners(2)	2,151,000	233,952
Entities affiliated with Venrock(3)	1,381,200	150,225
Lilly Ventures Fund I LLC(4)	1,072,800	116,594
Entities affiliated with Lux Capital(5)	530,081	57,654
William H. Rastetter(6)	27,600	3,002

(1) The 2014 convertible notes convert at 77.5% of the initial public offering price. The number of shares of common stock issuable upon conversion of our 2014 convertible notes is determined based on an assumed initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and assuming this offering is completed on April 15, 2014.

(2) Consists of 2014 convertible notes issued and sold to (a) Polaris Venture Partners V, L.P. in a principal amount of $2,075,573, (b) Polaris Venture Partners Entrepreneurs' Fund V, L.P. in a principal amount of $40,453, (c) Polaris Venture Partners Founders' Fund V, L.P. in a principal amount of $14,218 and (d) Polaris Venture Partners Special Founders' Fund V, L.P. in a principal amount of $20,756. Alan Crane, a member of our board of directors, is a general partner of Polaris Venture Partners, an affiliate of Polaris Venture Partners V, L.P., Polaris Venture Partners Entrepreneurs' Fund V, L.P., Polaris Venture Partners Founders' Fund V, L.P. and Polaris Venture Partners Special Founders' Fund V, L.P.

(3) Consists of 2014 convertible notes issued and sold to (a) Venrock Associates V, L.P. in a principal amount of $1,246,257, (b) Venrock Partners V, L.P. in a principal amount of $105,662 and (c) Venrock Entrepreneurs Fund V, L.P. in a principal amount of $29,281.

(4) Steven E. Hall, a member of our board of directors, is a venture partner of Lilly Ventures Fund I LLC.

(5) Consists of 2014 convertible notes issued and sold to (a) Lux Ventures II, L.P. in a principal amount of $479,876, (b) Lux Ventures II Sidecar, L.P. in a principal amount of $20,124 and (c) Lux Ventures II Partners Fund I LLC in a principal amount of $30,081.

(6) Consists of 2014 convertible notes issued and sold to William H. Rastetter and Marisa G. Rastetter as community property. Dr. Rastetter is a member of our board of directors.

Registration Rights

We are party to a second Series D convertible preferred stock purchase agreement with the holders of our preferred stock, including some of our directors and 5% stockholders and their affiliates and entities affiliated with certain of our directors. The second Series D convertible preferred stock purchase agreement provides these holders the right, following the closing of this offering, to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. See "Description of Capital Stock—Registration Rights" for additional information regarding these rights.

Participation in Offering

Certain of our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to $18.0 million of shares of common stock in this offering at the initial public offering price. Assuming an initial public offering price of $12.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, these stockholders would purchase an aggregate of up to approximately 1,500,000 of the 5,000,000 shares offered in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these existing principal stockholders and any of these existing principal stockholders could determine to purchase more, fewer or no shares in this offering.

Indemnification Agreements

Our certificate of incorporation, which will become effective upon the closing of this offering, provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with our directors. See "Executive Compensation—Limitation of Liability and Indemnification" for additional information regarding these agreements.

Policies and Procedures for Related Person Transactions

In connection with this offering, our board of directors adopted a written related person transaction policy that sets forth policies and procedures for the review and approval or ratification of related person transactions. Effective upon the closing of this offering, this policy will cover any transaction, arrangement or relationship in which we were or are to be a participant, the amount involved exceeds $120,000, and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a “related person,” had or will have a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a “related person transaction,” the related person must report the proposed related person transaction to our general counsel, or if we do not have a general counsel, our chief financial officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the audit committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the committee to review and, if deemed appropriate, approve proposed related person transactions that arise between audit committee meetings, subject to ratification by the audit committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person’s interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person’s interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person’s interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in our best interests. The audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC’s related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person’s position as an executive officer of another entity (whether or not the person is also a director of such entity), that is a participant in the transaction, where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, (b) the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction, and (c) the amount involved in the transaction equals less than the greater of $200,000 dollars or 5% of the annual gross revenues of the company receiving payment under the transaction; and
- a transaction that is specifically contemplated by provisions of our certificate of incorporation or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by our compensation committee in the manner specified in its charter.

We did not have a written policy regarding the review and approval of related person transactions prior to this offering. Nevertheless, with respect to such transactions, it has been the practice of our board of directors to consider the nature or and business reason for such transactions, how the terms of such transactions compared to those which might be obtained from unaffiliated third parties and whether such transactions were otherwise fair to and in our best interests.

PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock, as of February 28, 2014 by:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;
- each of our directors;
- each of our named executive officers; and
- all of our current executive officers and directors as a group.

The column entitled “Shares Beneficially Owned Prior to Offering—Percentage” is based on a total of 7,612,345 shares of our common stock outstanding as of February 28, 2014, including 6,826,019 shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering, but does not give effect to the conversion, as described below, of (1) an aggregate principal amount of $8.8 million and all accrued but unpaid interest on our 2013 convertible notes upon the closing of this offering or (2) an aggregate principal amount of $8.5 million and all accrued but unpaid interest on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering. The column entitled “Shares Beneficially Owned After Offering—Percentage” is based on shares of our common stock to be outstanding after this offering, including (a) the 5,000,000 shares of our common stock that we are selling in this offering, (b) the conversion of an aggregate principal amount of $8.8 million and all accrued but unpaid interest outstanding on our 2013 convertible notes upon the closing of this offering into an aggregate of 769,594 shares of our common stock, assuming an initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014 and (c) the conversion of an aggregate principal amount of $8.5 million and all accrued but unpaid interest outstanding on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering into an aggregate of 923,377 shares of our common stock, assuming an initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014, but not including any additional shares issuable upon exercise of outstanding options or warrants.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options or warrants that are currently exercisable or exercisable within 60 days of February 28, 2014 are considered outstanding and beneficially owned by the person holding the options or warrants for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o Cerulean Pharma Inc., 840 Memorial Drive, Cambridge, Massachusetts 02139.

Certain of our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to $18.0 million of shares of common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these existing principal stockholders and any of these existing principal stockholders could determine to purchase more, fewer or no shares in this offering.

The following table does not reflect any potential purchases by these existing principal stockholders or their affiliated entities. If any shares are purchased by these stockholders, the number and percentage of shares of our common stock beneficially owned by them after this offering will differ from those set forth in the following table.

	Shares Beneficially Owned Prior to Offering		Shares Beneficially Owned After Offering	
Name and address of Beneficial Owner	**Number**	**Percentage**	**Number**	**Percentage**
5% Stockholders				
Entities affiliated with Polaris Partners(1)	2,467,898	32.3%	2,926,687	20.4%
Entities affiliated with Venrock(2)	1,584,722	20.8%	1,879,323	13.1%
Entities affiliated with Lux Capital(3)	718,126	9.4%	797,584	5.6%
Entities affiliated with Lilly Ventures(4)	1,230,699	16.2%	1,459,415	10.2%
Entities affiliated with Crown Ventures(5)	830,481	10.9%	1,181,245	8.3%
Named Executive Officers and Directors				
Oliver S. Fetzer, Ph.D.(6)	267,132	3.4%	267,132	1.8%
Christopher D. T. Guiffre, J.D.(7)	34,283	*	34,283	*
Edward Garmey, M.D.(8)	40,796	*	40,796	*
Alan L. Crane(9)	2,562,332	33.5%	3,021,121	21.0%
Paul A. Friedman, M.D.	—	—	—	—
Steven E. Hall, Ph.D.(10)	1,230,699	16.2%	1,459,415	10.2%
William T. McKee	—	—	—	—
William H. Rastetter, Ph.D.(11)	31,718	*	37,610	*
Ram Sasisekharan, Ph.D.(12)	82,715	1.1%	82,715	*
Robert I. Tepper, M.D.(13)	21,108	*	21,108	*
All current executive officers and directors as a group(14)	4,302,221	53.5%	4,995,618	33.9%

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* Represents beneficial ownership of less than one percent of our outstanding common stock.

(1) Consists of (a) 178,061 and 3,338 shares of common stock issuable upon conversion of Seed convertible preferred stock held by Polaris Venture Partners IV, LP (“Polaris IV”) and Polaris Ventures Partners Entrepreneurs’ Fund IV, LP (“Polaris EFund IV”), respectively; (b) 348,769 and 6,538 shares of common stock issuable upon conversion of Series A convertible preferred stock held by Polaris IV and Polaris EFund IV, respectively; (c) 180,923 and 3,391 shares of common stock issuable upon conversion of Series B convertible preferred stock held by Polaris IV and Polaris EFund IV, respectively; (d) 451,844, 8,806, 3,095 and 4,518 shares of common stock issuable upon conversion of Series B-1 convertible preferred stock held by Polaris Venture Partners V, LP (“Polaris V”), Polaris Venture Partners Entrepreneurs’ Fund V, LP (“Polaris EFund V”), Polaris Ventures Partners Founders’ Fund V, LP (“Polaris FFund V”) and Polaris Venture Partners Special Founders’ Fund V, LP (“Polaris SFFund V” and together with Polaris IV, Polaris EFund IV, Polaris V, Polaris EFund V and Polaris FFund V, the “Polaris Funds”), respectively; (e) 489,289, 9,172, 151,549, 2,953, 1,038 and 1,515 shares of common stock issuable upon conversion of Series C convertible preferred stock held by Polaris IV, Polaris Efund IV, Polaris V, Polaris EFund V, Polaris FFund V and Polaris SFFund V, respectively; (f) 208,709, 3,912, 366,720, 7,147, 2,512 and 3,667 shares of common stock issuable upon conversion of Series D convertible preferred stock held by Polaris IV, Polaris EFund IV, Polaris V, Polaris EFund V, Polaris FFund V and Polaris SFFund V, respectively and (g) 5,242, 98, 24,214, 471, 165 and 242 shares of common stock issuable upon conversion of shares of Series C convertible preferred stock issuable upon the exercise of warrants held by Polaris IV, Polaris EFund IV, Polaris V, Polaris EFund V, Polaris FFund V and Polaris SFFund V, respectively. Shares beneficially owned after this offering also includes (a) 216,953, 4,228, 1,486 and 2,170 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2013 convertible notes held by Polaris V, Polaris Efund V, Polaris FF Fund V and Polaris SFFund V, respectively, and (b) 225,748, 4,400, 1,546 and 2,258 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2014 convertible notes held by Polaris V, Polaris Efund V, Polaris FF Fund V and Polaris SFFund V, respectively. Each of the Polaris Funds has the sole voting and investment power with respect to the shares directly held by it. The general partner of

each of Polaris IV and Polaris EFund IV is Polaris Venture Management Co. IV, LLC (“Polaris Management IV”). The general partner of each of Polaris V, Polaris EFund V, Polaris FFund V and Polaris SFFund V is Polaris Venture Management Co. V, LLC (“Polaris Management V”). Each of Polaris Management IV and Polaris Management V may be deemed to have sole voting and investment power with respect to the shares held by the Polaris Funds of which they are general partner, and each of Polaris Management IV and Polaris Management V disclaim beneficial ownership of all the shares held by such Polaris Funds except to the extent of their proportionate pecuniary interests therein. North Star Venture Management 2000, LLC (“North Star”) directly or indirectly provides investment advisory services to various venture capital funds, including the Polaris Funds. The members of North Star (the “Management Members”) are also members of Polaris Management IV and Polaris Management V, and as such, they may be deemed to share voting and investment power over the shares held by the Polaris Funds. The Management Members disclaim beneficial ownership of such shares, except to the extent of their proportionate pecuniary interest therein. Alan Crane, one of our directors, has an assignee interest in Polaris Management IV and Polaris Management V. To the extent that he is deemed to share voting and investment powers with respect to the shares held by the Polaris Funds, Mr. Crane disclaims beneficial ownership of all the shares held by the Polaris Funds except to the extent of his proportionate pecuniary interest therein. The mailing address of the beneficial owner is c/o Polaris Venture Partners, 1000 Winter Street, Suite 3350, Waltham, MA 02451.

(2) Consists of (a) 320,594, 27,181 and 7,532 shares of common stock issuable upon conversion of Series A convertible preferred stock held by Venrock Associates V, LP (“VA5”), Venrock Partners V, LP (“VP5”) and Venrock Entrepreneurs V, LP (“VE5” and collectively with VA5 and VP5, the “Venrock Funds”), respectively; (b) 116,241, 9,855 and 2,731 shares of common stock issuable upon conversion of Series B convertible preferred stock held by VA5, VP5 and VE5, respectively; (c) 264,082, 22,389 and 6,204 shares of common stock issuable upon conversion of Series B-1 convertible preferred stock held by VA5, VP5 and VE5, respectively; (d) 369,699, 31,344 and 8,686 shares of common stock issuable upon conversion of Series C convertible preferred stock held by VA5, VP5 and VE5, respectively; (e) 342,119, 29,005 and 8,038 shares of common stock issuable upon conversion of Series D convertible preferred stock held by VA5, VP5 and VE5, respectively and (f) 17,164, 1,455 and 403 shares of common stock issuable upon conversion of Series C convertible preferred stock issuable upon the exercise of warrants held by VA5, VP5 and VE5, respectively. Shares beneficially owned after this offering also includes (a) 130,270, 11,405 and 3,061 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2013 convertible notes held by VA5, VP5 and VE5, respectively, and (b) 135,548, 11,492 and 3,185 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2014 convertible notes held by VA5, VP5 and VE5, respectively. Venrock Management V, LLC (“VM5”), Venrock Partners Management V, LLC (“VPM5”) and VEF Management V, LLC (“VEFM5”) are the sole general partners of VA5, VP5 and VEF5, respectively, and may be deemed to own the shares held by the Venrock Funds. VM5, VPM5 and VEFM5 disclaim beneficial ownership of all the shares held by the Venrock Funds except to the extent of their proportionate pecuniary interest therein. The mailing address of the beneficial owner is 3340 Hillview Ave., Palo Alto, CA 94304.

(3) Consists of (a) 136,402 and 5,720 shares of common stock issuable upon conversion of Series A convertible preferred stock held by Lux Ventures II, LP (“Lux II”) and Lux Ventures II Sidecar, LP (“Lux II Sidecar”), respectively; (b) 76,569 and 3,211 shares of common stock issuable upon conversion of Series B convertible preferred stock held by Lux II and Lux II Sidecar, respectively; (c) 126,412 and 5,301 shares of common stock issuable upon conversion of Series B-1 convertible preferred stock held by Lux II and Lux II Sidecar, respectively; (d) 151,970, 26,081 and 6,372 shares of common stock issuable upon conversion of Series C convertible preferred stock held by Lux II, Lux Ventures II Partners Fund I LLC (“Lux II Partners”) and Lux II Sidecar, respectively; (e) 156,529, 8,434 and 6,594 shares of common stock issuable upon conversion of Series D convertible preferred stock held by Lux II, Lux II Partners and Lux II Sidecar, respectively and (f) 8,217 and 344 of common stock issuable upon conversion of Series C convertible preferred stock issuable upon the exercise of warrants held by Lux II and Lux II Sidecar, respectively. Lux Venture Partners II, L.P. Shares beneficially owned after this offering also includes (a) 19,898, 1,072 and 834 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2013 convertible notes held by Lux, Lux II Partners and Lux II Sidecar,

respectively, and (b) 52,193, 3,272 and 2,189 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2014 convertible notes held by Lux, Lux II Partners and Lux II Sidecar, respectively. Lux Venture Partners II, L.P. (“Lux Venture Partners”) is (i) the general partner of Lux II and Lux II Sidecar and (ii) the manager of Lux II Partners. Lux Venture Associates II, LLC (“Lux Associates”) is the general partner of Lux Venture Partners and Lux Capital Management, LLC (“Lux Management”) is the sole member of Lux Venture Partners. Robert Paull, Joshua Wolfe and Peter Hebert are the individual managers of Lux Management (the “Individual Managers”). Lux Venture Partners, Lux Associates and Lux Management disclaim beneficial ownership of such shares, except to the extent of their pecuniary interest therein. Lux Management, as sole member, may be deemed to share voting and investment powers for the shares held by Lux II and Lux II Sidecar. As one of three individual managers, each of the Individual Managers disclaims beneficial ownership over the shares reported herein, and in all events disclaims beneficial ownership except to the extent of his pecuniary interest therein. The mailing address of the beneficial owner is 295 Madison Ave., 24th Floor, New York, NY 10017.

(4) Consists of (a) 931,486 shares of common stock issuable upon conversion of Series C convertible preferred stock and (b) 299,213 shares of common stock issuable upon conversion of Series D convertible preferred stock. Shares beneficially owned after this offering also includes 112,122 and 116,594 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2013 convertible notes and 2014 convertible notes, respectively. Steven E. Hall is a venture partner at Lilly Ventures Fund I LLC and has shared voting and shared investment power over such shares, and may be deemed the indirect beneficial owner of such shares. Dr. Hall disclaims beneficial ownership over such shares, except to the extent of any pecuniary interest therein. The mailing address of the beneficial owner is 115 W. Washington Street, Suite 1680-South, Indianapolis, IN 46204.

(5) Consists of 830,481 shares of common stock issuable upon conversion of Series D convertible preferred stock held by CVF, LLC. Shares beneficially owned after this offering also includes 261,651 and 89,113 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2013 convertible notes and 2014 convertible notes, respectively. Richard H. Robb, manager of CVF, LLC, exercises voting and investment power with respect to shares held by CVF, LLC. Mr. Robb disclaims beneficial ownership of all shares held by CVF, LLC except to the extent of his pecuniary interest therein. The mailing address of the beneficial owner is 222 N. LaSalle Street, Suite 2000, Chicago, IL 60601.

(6) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.

(7) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.

(8) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.

(9) Consists of (a) the shares described in note (1) above, (b) 77,201 shares of common stock and (c) 17,233 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.

(10) Consists of the shares described in note (4) above. Dr. Hall is a venture partner at Lilly Ventures Fund I and has shared voting and shared investment power over such shares, and may be deemed the indirect beneficial owner of such shares. Dr. Hall disclaims beneficial ownership over such shares, except to the extent of any pecuniary interest therein.

(11) Consists of (a) 7,106 shares of common stock issuable upon conversion of Series A convertible preferred stock; (b) 2,576 shares of common stock issuable upon conversion of Series B convertible preferred stock; (c) 5,868 shares of common stock issuable upon conversion of Series B-1 convertible preferred stock; (d) 8,199 shares of common stock issuable upon conversion of Series C convertible preferred stock; (e) 7,589 shares of common stock issuable upon conversion of Series D convertible preferred stock and (f) 380 shares of common stock issuable upon conversion of Series C convertible preferred stock issuable upon the exercise of warrants. Shares beneficially owned after this offering also includes 2,890 and 3,002 shares of common stock issuable upon conversion of principal and accrued interest outstanding on our 2013 convertible notes and 2014 convertible notes, respectively. William H. Rastetter holds the aforementioned shares jointly as community property with his wife.

(12) Consists of shares of common stock.

(13) Consists of (a) 18,954 shares of common stock and (b) 2,154 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.

(14) Includes 393,036 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2014.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries and are qualified by reference to the certificate of incorporation and bylaws that will become effective upon the closing of this offering. Copies of these documents have been filed with the Securities and Exchange Commission as exhibits to our registration statement, of which this prospectus forms a part. The description of our common stock reflects changes to our capital structure that will occur upon the closing of this offering.

Following the closing of this offering, our authorized capital stock will consist of 120,000,000 shares of common stock, par value $0.0001 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share, all of which preferred stock will be undesignated.

As of February 28, 2014, we had issued and outstanding:

- 786,326 shares of our common stock, held by 41 stockholders of record;
- 2,500,000 shares of our Seed preferred stock that will automatically convert into 181,399 shares of our common stock upon the closing of this offering, held by 2 stockholders of record;
- 9,307,692 shares of our Series A preferred stock that will automatically convert into 859,842 shares of our common stock upon the closing of this offering, held by 8 stockholders of record;
- 3,562,000 shares of our Series B preferred stock that will automatically convert into 402,559 shares of our common stock upon the closing of this offering, held by 9 stockholders of record;
- 4,842,500 shares of our Series B-1 preferred stock that will automatically convert into 902,151 shares of our common stock upon the closing of this offering, held by 11 stockholders of record;
- 31,836,392 shares of our Series C preferred stock that will automatically convert into 2,194,476 shares of our common stock upon the closing of this offering, held by 15 stockholders of record; and
- 33,158,272 shares of our Series D preferred stock that will automatically convert into 2,285,592 shares of our common stock upon the closing of this offering, held by 16 stockholders of record.

Upon the closing of this offering, all of the outstanding shares of our preferred stock will automatically convert into an aggregate of 6,826,019 shares of our common stock.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our certificate of incorporation that will become effective upon the closing of this offering, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Stock Options

As of February 28, 2014, options to purchase 1,215,315 shares of our common stock at a weighted-average exercise price of $4.84 per share were outstanding.

Warrants

As of February 28, 2014, we had outstanding:

- a warrant to purchase 15,000 shares of our Series B preferred stock, or the Series B warrant, at an exercise price of $2.00 per share;
- warrants to purchase an aggregate of 878,370 shares of our Series C preferred stock, or the Series C warrants, at an exercise price of $0.74 per share; and
- a warrant to purchase 963,856 shares of our Series D preferred stock, or the Series D warrant, at an exercise price of $0.83 per share.

Upon the closing of this offering, and after giving effect to the automatic conversion of our preferred stock into common stock, (1) the Series B warrant will be exercisable, at the election of the holder, for an aggregate of 1,695 shares of our common stock, at an exercise price of $17.70 per share, (2) the Series C warrants will be exercisable, at the election of the holders, for an aggregate of 60,539 shares of our common stock, at an exercise price of $10.74 per share, and (3) the Series D warrant will be exercisable, at the election of the holder, for an aggregate of 66,438 shares of our common stock, at an exercise price of $12.04 per share. All of the warrants provide for adjustments in the event of specified mergers, reorganizations, reclassifications, stock dividends, stock splits or other changes in our corporate structure. The Series B warrant expires on August 8, 2018, the Series C warrants expire on November 12, 2017 and the Series D warrant expires on December 6, 2021.

Convertible Promissory Notes

In 2013, we issued and sold convertible promissory notes in an aggregate principal amount of $8.8 million. We refer to these notes as our 2013 convertible notes. Our 2013 convertible notes bear interest at an annual rate of 7% and are payable after one year upon demand made by the holders of at least 60% of the aggregate principal amount outstanding under our 2013 convertible notes. Upon the closing of this offering, all principal and accrued interest under our 2013 convertible notes will convert into an aggregate of 769,594 shares of common stock, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014. For more information on the 2013 convertible notes, see “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources—Indebtedness.”

In 2014, we issued and sold 7% convertible promissory notes in an aggregate principal amount of $8.5 million. We refer to these notes as our 2014 convertible notes. Our 2014 convertible notes bear interest at an annual rate of 7% and are payable after February 26, 2015 upon demand made by the holders of at least 60% of the aggregate principal amount outstanding under our 2014 convertible notes. Upon closing of this offering, all principal and accrued interest under our 2014 convertible notes, which convert at 77.5% of the initial public offering price, will convert into an aggregate of 923,377 shares of our common stock, assuming an initial public offering price per share of $12.00, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that the offering closes on April 15, 2014.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware law

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a “business combination” with any “interested stockholder” for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A “business combination” includes, among other things, a merger or consolidation involving us and the “interested stockholder” and the sale of more than 10% of our assets. In general, an “interested stockholder” is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders that will own 15% or more of our outstanding voting stock upon the closing of this offering.

Staggered board; removal of directors

Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, a director may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Super-majority voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation’s certificate of incorporation or by-laws, unless a corporation’s certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our by-laws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast in an annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes which all our stockholders would be entitled to cast in an election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation relating to the classification of our board of directors and the limitations on the removal of directors and filling of vacancies.

Stockholder action; special meeting of stockholders; advance notice requirements for stockholder proposals and director nominations

Our certificate of incorporation provides that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of such stockholders and may not be effected by any consent in writing by such stockholders. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our Chairman of the Board, our Chief Executive Officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Authorized but unissued shares

The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of the NASDAQ Global Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Registration Rights

We have entered into a second Series D convertible preferred stock purchase agreement, dated November 30, 2012, which we refer to as the second Series D purchase agreement, with the holders of our preferred stock, certain holders of our common stock, and the holders of the Series B warrant and the Series D warrant. Upon the closing of this offering, holders of a total of 7,638,324 shares of our common stock as of December 31, 2013, including shares issuable upon conversion of our preferred stock and upon exercise of the Series B warrant, the Series C warrants and the Series D warrant, will have the right to require us to register these shares under the Securities Act of 1933, as amended, or Securities Act, and/or to participate in future registrations of securities by us, under the circumstances described below. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. If not otherwise exercised, the rights described below will expire five years after the closing of this offering.

Demand registration rights

Beginning 180 days after the effective date of the registration statement of which this prospectus forms a part, subject to specified limitations set forth in the second Series D purchase agreement, at any time, the holders of 58% of the then-outstanding shares will have registration rights under the second Series D purchase agreement, which we refer to as registrable shares, may at any time demand in writing that we register all or a portion of the registrable shares under the Securities Act. We are not obligated to file a registration statement pursuant to this provision on more than two occasions, and we may defer the filing of a registration for a period of not more than 90 days if we determine in good faith that it would be seriously detrimental to us for a registration statement to be filed.

Form S-3 registration rights

In addition, at any time after we become eligible to file a registration statement on Form S-3, subject to specified limitations set forth in the second Series D purchase agreement, the holders of registrable shares may demand in writing that we register on Form S-3 all or a portion of the registrable shares so long as the total amount of registrable shares being registered has an aggregate price to the public of at least $1 million. We are not obligated to file a Form S-3 pursuant to this provision on more than two occasions in any 12-month period, and we may defer the filing of the Form S-3 registration statement for a period of up to sixty days if in the good faith judgment of the underwriters it would be seriously detrimental to us for the Form S-3 registration to be filed.

Incidental registration rights

If, at any time after the closing of this offering, we propose to file a registration statement under the Securities Act, subject to specified exceptions, the holders of registrable shares will be entitled to notice of the registration and have the right to require us to register all or a portion of the registrable shares then held by them.

In the event that any registration in which the holders of registrable shares elect to participate pursuant to the second Series D purchase agreement is intended to be an underwritten public offering, we have agreed to enter into an underwriting agreement in usual and customary form. Holders of registrable securities must agree to any such underwriting agreement as a condition to participation in the offering.

In the event that any registration in which the holders of registrable shares participate pursuant to the second Series D purchase agreement is an underwritten public offering, we will use our best efforts to include the requested registrable shares to be included, but may be limited by market conditions.

Expenses

Pursuant to the second Series D purchase agreement, we are required to pay all registration expenses, including registration and filing fees, exchange listing fees, printing expenses and accounting fees and the fees and expenses of one counsel to represent the selling stockholders, other than any underwriting discounts and commissions, that are related to any demand, Form S-3 or incidental registration described above. The second Series D purchase agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be American Stock Transfer & Trust Company, LLC.

NASDAQ Global Market

We have applied to have our common stock listed on the NASDAQ Global Market under the symbol “CERU.”

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and a liquid trading market for our common stock may not develop or be sustained after this offering. Future sales of substantial amounts of common stock in the public market, including shares issued upon exercise of outstanding options, or the anticipation of these sales, could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through sales of equity securities. We have applied to have our common stock listed on The NASDAQ Global Market under the symbol “CERU.”

Upon the closing of this offering, we will have outstanding an aggregate of 14,305,316 shares of common stock, assuming (1) the issuance of 5,000,000 shares of common stock offered by us in this offering, (2) the conversion of all outstanding shares of our preferred stock into 6,826,019 shares of our common stock upon the closing of this offering, (3) the conversion of all principal and accrued interest on our 2013 convertible notes upon the closing of this offering, assuming an initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus and that this offering closes on April 15, 2014, and (4) the conversion of all principal and accrued interest outstanding on our 2014 convertible notes, which convert at 77.5% of the initial public offering price, upon the closing of this offering, assuming an initial public offering price of $12.00 per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, and that this offering closes on April 15, 2014, and assuming no exercise of options or warrants after February 28, 2014. Of the shares to be outstanding immediately after the closing of this offering, the 5,000,000 shares sold in this offering (assuming that the underwriters do not exercise their overallotment option) will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our “affiliates,” as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining 9,305,316 shares of common stock will be “restricted securities,” as that term is defined in Rule 144 under the Securities Act and will further be subject to either restrictions on transfer under the lock-up agreements described below or restrictions on transfer for a period of 180 days from the effectiveness of the registration statement of which this prospectus forms a part under stock option agreements entered into between us and the holders of those shares. Following the expiration of these restrictions, these shares will become eligible for public sale if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below.

In addition, of the 1,215,315 shares of our common stock that were subject to stock options outstanding as of February 28, 2014, options to purchase 629,895 shares of common stock were vested and exercisable as of February 28, 2014. Upon exercise, these shares will be eligible for sale subject to the lock–up agreements and securities law restrictions described below. All of the 128,672 shares of common stock subject to our outstanding warrants as of December 31, 2013 were exercisable as of December 31, 2013 and upon issuance these shares will be eligible for sale, subject to the lock-up agreements and securities laws described below.

Lock-Up Agreements

We and each of our directors and executive officers and holders of substantially all of our outstanding capital stock, who collectively own approximately 97% of the shares of our common stock, based on shares outstanding as of December 31, 2013, have agreed that, without the prior written consent of Leerink Partners LLC, on behalf of the underwriters, we and they will not, subject to limited exceptions, during the period ending 180 days after the date of this prospectus, subject to extension in specified circumstances:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock,

whether any transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise.

The lock-up restrictions, specified exceptions and the circumstances under which the lock-up period may be extended are described in more detail in the section of this prospectus entitled “Underwriting.”

Upon the expiration of the applicable lock-up periods, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above.

Rule 144

Affiliate resales of restricted securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in “broker’s transactions” or certain “riskless principal transactions” or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 143,053 shares immediately after this offering, assuming no exercise of the underwriter’s option to purchase additional shares; or
- the average weekly trading volume in our common stock on the NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the Securities and Exchange Commission and NASDAQ concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-affiliate resales of restricted securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the three months preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of an issuer’s employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The Securities and Exchange Commission has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

Equity Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issued or issuable under our stock plans. We expect to file the registration statement covering shares offered pursuant to our stock plans shortly after the date of this prospectus, permitting the resale of such shares by nonaffiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

Registration Rights

Upon the closing of this offering, the holders of 7,638,324 shares of common stock or their transferees will be entitled to various rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See “Description of Capital Stock—Registration Rights” for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of the lock-up agreement.

Participation in Offering

Certain of our existing principal stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to $18.0 million of shares of common stock in this offering at the initial public offering price. Any such shares purchased by these potential purchasers may not be able to be resold in the public market immediately following this offering as a result of restrictions under securities laws and lock-up agreements, but would be able to be sold following the expiration of these restrictions, in each case as described above. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering, and the foregoing discussion does not reflect any potential purchases by these potential purchasers.

MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a general discussion of material U.S. federal income and estate tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury regulations.

An individual may be treated as a resident instead of a nonresident of the United States in any calendar year for U.S. federal income tax purposes if the individual was present in the United States for at least 31 days in that calendar year and for an aggregate of at least 183 days during the three-year period ending with the current calendar year. For purposes of this calculation, all of the days present in the current year, one-third of the days present in the immediately preceding year and one-sixth of the days present in the second preceding year are counted. Residents are taxed for U.S. federal income tax purposes as if they were U.S. citizens.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- controlled foreign corporations;
- passive foreign investment companies;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and
- certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or persons who hold their common stock through partnerships or other entities which are transparent for U.S. federal income tax purposes. A partner in a partnership or other transparent entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other transparent entity, as applicable.

Prospective investors should consult their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of our common stock.

Dividends

As discussed in the "Dividend Policy" section of this prospectus, we do not expect to pay dividends in the foreseeable future. If we pay distributions on our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Disposition of Common Stock."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder provides a valid IRS Form W-8ECI (or an acceptable substitute form). However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on Disposition of Common Stock

A non-U.S. holder generally will not be subject to U.S. federal income tax on gain recognized on a disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;

- the non-U.S. holder is an individual present in the United States for 183 days or more in the taxable year of the disposition and some other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition; or
- we are or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation" unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes.

Information Reporting and Backup Withholding Tax

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate, currently 28%, with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

Federal Estate Tax

Common stock owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Recently Enacted Legislation Relating to Foreign Accounts

The Foreign Account Tax Compliance Act, or FATCA, was enacted in March 2010. Generally, FATCA imposes a 30% withholding tax on dividends of, and gross proceeds from the sale or disposition, of our common stock if paid to a foreign entity unless (i) if the foreign entity is a “foreign financial institution,” the foreign entity undertakes certain due diligence, reporting, withholding, and certain certification obligations, (ii) if the foreign entity is not a “foreign financial institution,” the foreign entity identifies certain of its U.S. investors, or (iii) the foreign entity is otherwise exempt under FATCA.

Although this legislation is effective with regards to amounts paid after December 31, 2012, (1) under IRS Notice 2013-43 issued on July 7, 2013, withholding under FATCA will only apply to payments of dividends on our common stock made after June 30, 2014 and (2), under final regulations issued by the U.S. Department of Treasury on January 17, 2013, to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2016. Under certain circumstances, a non-US holder may be eligible for refunds or credits of the tax. Non-U.S. holders should consult their own tax advisors regarding the possible implications of this legislation on their investment in our common stock.

The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non- U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

UNDERWRITING

Leerink Partners LLC is acting as representative of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Leerink Partners LLC	
Canaccord Genuity Inc.	
JMP Securities LLC	
Wedbush Securities Inc.	
Total	5,000,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representative has advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover of this prospectus and to dealers at that price less a concession not in excess of $ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

The expenses of the offering, not including the underwriting discount, are estimated at $2.8 million and are payable by us. We have agreed to reimburse the underwriters in an amount not to exceed $50,000 for expenses related to the clearing of this offering with the Financial Industry Regulatory Authority and all expenses relating to the qualification of our common stock under state securities laws.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to 750,000 additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors and all of our other existing security holders have agreed not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 180 days after the date of this prospectus without first obtaining the written consent of Leerink Partners LLC. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- request or demand that we file a registration statement related to the common stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

NASDAQ Global Market Listing

We have applied to list our common stock on the NASDAQ Global Market, subject to notice of issuance, under the symbol "CERU."

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representative. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representative believes to be comparable to us;
- our financial information;
- the history of, and the prospects for, our company and the industry in which we compete;
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues;
- the present state of our development; and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representative may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option described above. The underwriters may close out any covered short position by either exercising their option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. “Naked” short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representative has repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the NASDAQ Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representative will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They may in the future receive customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers.

Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a “Relevant Member State”), no offer of shares may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representative; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require the Company or the representative to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a “qualified investor” within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representative has been obtained to each such proposed offer or resale.

The company, the representative and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression “an offer to the public” in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Ropes & Gray LLP, Boston, Massachusetts, has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

EXPERTS

The consolidated financial statements as of December 31, 2012 and 2013, and for the years then ended, included in this prospectus, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein (which report expresses an unqualified opinion on the consolidated financial statements and includes an explanatory paragraph referring to our ability to continue as a going concern). Such consolidated financial statements have been so included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock we are offering to sell. This prospectus, which constitutes part of the registration statement, does not include all of the information contained in the registration statement and the exhibits, schedules and amendments to the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits and schedules to the registration statement. Statements contained in this prospectus about the contents of any contract, agreement or other document are not necessarily complete, and, in each instance, we refer you to the copy of the contract, agreement or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference to such contract, agreement or document.

You may read and copy the registration statement of which this prospectus is a part at the SEC’s public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. You can request copies of the registration statement by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC’s public reference room. In addition, the SEC maintains an Internet website, which is located at www.sec.gov, that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. You may access the registration statement of which this prospectus is a part at the SEC’s Internet website.

Upon closing of this offering, we will be subject to the informational and periodic reporting requirements of the Exchange Act. We will fulfill our obligations with respect to such requirements by filing periodic reports and other information with the SEC. We intend to furnish our stockholders with annual reports containing consolidated financial statements certified by an independent registered public accounting firm. We also maintain a website at www.ceruleanrx.com. The information contained in, or which can be accessed through, our website does not constitute a part of this prospectus.

CERULEAN PHARMA INC.
(A Development Stage Company)

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Cerulean Pharma Inc.
Cambridge, Massachusetts

We have audited the accompanying consolidated balance sheets of Cerulean Pharma Inc. (a development stage company) and subsidiary (the “Company”) as of December 31, 2012 and 2013, and the related consolidated statements of operations, redeemable convertible preferred stock and stockholders’ deficit, and cash flows for the years then ended and for the period from November 28, 2005 (date of incorporation) to December 31, 2013. These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Cerulean Pharma Inc. and subsidiary as of December 31, 2012 and 2013, and the results of their consolidated operations and their cash flows for the years then ended and for the period November 28, 2005 (date of incorporation) to December 31, 2013, in conformity with accounting principles generally accepted in the United States of America.

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company’s recurring losses from operations, working capital deficiency and accumulated deficit raise substantial doubt about its ability to continue as a going concern. Management’s plans in regard to these matters are also described in Note 1 to the consolidated financial statements. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 7, 2014 (March 31, 2014 as to the effects
of the reverse stock split described in Note 18)

CERULEAN PHARMA INC.
(A Development Stage Company)

CONSOLIDATED BALANCE SHEETS

	December 31, 2012	December 31, 2013	Pro Forma December 31, 2013 (unaudited)
ASSETS			
Current assets:			
Cash and cash equivalents	$ 16,707,000	$ 5,488,000	$ 5,488,000
Accounts receivable, prepaid expenses, and other current assets	357,000	959,000	959,000
Total current assets	17,064,000	6,447,000	6,447,000
Property and equipment — Net	442,000	245,000	245,000
Other assets	155,000	135,000	135,000
Total	$ 17,661,000	$ 6,827,000	$ 6,827,000
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT			
Current liabilities:			
Current portion of loan payable	$ 2,869,000	$ 3,134,000	$ 3,134,000
Convertible promissory notes payable to shareholders	—	8,824,000	—
Accounts payable	900,000	914,000	914,000
Accrued expenses	2,741,000	2,274,000	2,040,000
Other liabilities	14,000	—	—
Total current liabilities	6,524,000	15,146,000	6,088,000
Long-term liabilities:			
Loan payable — net of current portion	6,258,000	3,124,000	3,124,000
Preferred stock warrant liability	1,130,000	928,000	—
Noncurrent accrued interest	37,000	391,000	391,000
Other	—	12,000	12,000
Total long-term liabilities	7,425,000	4,455,000	3,527,000
Redeemable convertible preferred stock (Note 8)	83,751,000	81,525,000	—
Commitments (Note 13)			
Stockholders' deficit:			
Common stock, $0.0001 par value; 132,000,000 shares and designated, 609,945 and 785,531 shares issued and outstanding at December 31, 2012 and 2013, respectively and 8,366,375 at December 31, 2013 (pro forma unaudited)	—	—	1,000
Additional paid-in capital	1,257,000	4,140,000	95,650,000
Deficit accumulated during the development stage	(81,296,000)	(98,439,000)	(98,439,000)
Total stockholders' deficit	(80,039,000)	(94,299,000)	(2,788,000)
Total	$ 17,661,000	$ 6,827,000	$ 6,827,000

See notes to consolidated financial statements.

CERULEAN PHARMA INC.
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF OPERATIONS

	Years Ended December 31,		Period from November 28, 2005 (Date of Incorporation) to December 31, 2013
	2012	2013	
Revenue	$ 625,000	$ 6,000	$ 1,669,000
Operating expenses:			
Research and development	15,807,000	9,700,000	67,042,000
General and administrative	6,393,000	6,166,000	31,570,000
Total operating expenses	22,200,000	15,866,000	98,612,000
Other income (expense):			
Interest income	2,000	2,000	684,000
Interest expense	(567,000)	(1,487,000)	(2,395,000)
Decrease in value of preferred stock warrant liability	39,000	202,000	215,000
Total other income (expense) — net	(526,000)	(1,283,000)	(1,496,000)
Net loss	(22,101,000)	(17,143,000)	(98,439,000)
Accretion of redeemable convertible preferred stock	(73,000)	—	(694,000)
Net loss attributable to common stockholders	$(22,174,000)	$(17,143,000)	$ (99,133,000)
Net loss per share attributable to common stockholders:			
Basic and diluted	$ (36.39)	$ (25.05)	$ (164.80)
Weighted-average common shares outstanding:			
Basic and diluted	609,344	684,330	601,547
Pro forma net loss per share attributable to common stockholders (unaudited):			
Basic and diluted		$ (2.14)	
Pro forma weighted-average common shares outstanding (unaudited):			
Basic and diluted		7,883,204	

See notes to consolidated financial statements.

CERULEAN PHARMA INC.
(A Development Stage Company)

CONSOLIDATED STATEMENT OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT

	Redeemable Convertible Preferred Stock $0.01 Par Value		Common Stock $0.0001 Par Value		Additional Paid-In Capital	Deficit Accumulated During the Development Stage	Total
	Shares	**Amount**	**Shares**	**Amount**			
OPENING BALANCE — November 28, 2005 (date of incorporation)	—	$ —	—	$ —	$ —	$ —	$ —
BALANCE — December 31, 2005	—	—	—	—	—	—	—
Issuance of founders' shares at $0.0001 per share			516,958		1,000		1,000
Issuance of common stock at $3.92 per share in accordance with a Patent License Agreement			36,270		142,000		142,000
Sale of Seed Convertible Preferred Stock at $0.80 per share, net of issuance cost of $83,000	2,500,000	1,917,000					
Net loss						(733,000)	(733,000)
BALANCE — December 31, 2006	2,500,000	1,917,000	553,228		143,000	(733,000)	(590,000)
Issuance of common stock at $4.64 per share in accordance with a Patent License Agreement			12,897		60,000		60,000
Vesting of restricted common stock at $3.92 per share			7,754		30,000		30,000
Sale of Series A Convertible Preferred Stock at $1.30 per share, net of issuance costs of $56,000	9,307,692	12,043,000					
Sale of Series B Convertible Preferred Stock at $2.00 per share, net of issuance costs of $45,000	4,062,500	8,080,000					
Stock-based compensation					28,000		28,000
Net loss						(5,238,000)	(5,238,000)
BALANCE — December 31, 2007	15,870,192	22,040,000	573,879		261,000	(5,971,000)	(5,710,000)
Exercise of stock options at $3.77 per share			3,446		13,000		13,000
Vesting of restricted common stock at $6.38 per share			7,754		49,000		49,000
Stock-based compensation					57,000		57,000
Net loss						(8,731,000)	(8,731,000)
BALANCE — December 31, 2008	15,870,192	22,040,000	585,079		380,000	(14,702,000)	(14,322,000)
Exercise of stock options at $3.77 per share			533		2,000		2,000
Vesting of restricted common stock at $5.95 per share			7,754		46,000		46,000
Sale of Series B-1 Convertible Preferred Stock at $2.00 per share, net of issuance costs of $75,000	5,000,000	9,925,000					
Stock-based compensation					191,000		191,000
Net loss						(12,700,000)	(12,700,000)
BALANCE — December 31, 2009	20,870,192	31,965,000	593,366		619,000	(27,402,000)	(26,783,000)
Exercise of stock options at $3.92 to $5.95 per share			982		5,000		5,000
Vesting of restricted common stock at $3.34 per share			7,754		26,000		26,000
Sale of Series C Convertible Preferred Stock at $0.74 per share, net of issuance costs of $264,000	13,276,114	9,560,000					
Conversion of shareholder notes and accrued interest into Series C Convertible Preferred Stock at $0.74 per share	9,021,175	6,203,000					
Stock-based compensation					211,000		211,000
Net loss						(12,851,000)	(12,851,000)

	Redeemable Convertible Preferred Stock $0.01 Par Value		Common Stock $0.0001 Par Value		Additional Paid-In Capital	Deficit Accumulated During the Development Stage	Total
	Shares	Amount	Shares	Amount			
BALANCE — December 31, 2010	43,167,481	47,728,000	602,102		861,000	(40,253,000)	(39,392,000)
Exercise of stock options at $3.34 to $5.95 per share			6,939		34,000		34,000
Sale of Series C Convertible Preferred Stock at $0.74 per share, net of issuance costs of $22,000	10,135,128	7,478,000					
Sale of Series D Convertible Preferred Stock at $0.83 per share, net of issuance costs of $76,000	18,072,287	14,924,000					
Stock-based compensation					524,000		524,000
Accretion of issuance costs to redemption value		621,000			(621,000)		(621,000)
Net loss						(18,942,000)	(18,942,000)
BALANCE — December 31, 2011	71,374,896	70,751,000	609,041		798,000	(59,195,000)	(58,397,000)
Exercise of stock options at $3.34 to $3.92 per share			904		3,000		3,000
Sale of Series D Convertible Preferred Stock at $0.83 per share, net of issuance costs of $73,000	15,662,650	12,927,000					
Stock-based compensation					529,000		529,000
Accretion of issuance costs to redemption value		73,000			(73,000)		(73,000)
Net loss						(22,101,000)	(22,101,000)
BALANCE — December 31, 2012	87,037,546	83,751,000	609,945		1,257,000	(81,296,000)	(80,039,000)
Exercise of stock options at $3.34 to $5.95 per share			8,911		35,000		35,000
Stock-based compensation					622,000		622,000
Conversion of preferred stock into common stock at $14.51 to $39.21 per share	(1,830,190)	(2,226,000)	166,675		2,226,000		2,226,000
Net loss						(17,143,000)	(17,143,000)
BALANCE — December 31, 2013	85,207,356	$ 81,525,000	785,531		$4,140,000	$(98,439,000)	$(94,299,000)

See notes to consolidated financial statements.

CERULEAN PHARMA INC.
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years Ended December 31,		Period from November 28, 2005 (Date of Incorporation) to December 31, 2013
	2012	2013	
Cash flows from operating activities:			
Net loss	$(22,101,000)	$(17,143,000)	$ (98,439,000)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	529,000	622,000	2,313,000
Noncash research and development expense	—	—	202,000
Noncash rent expense	(68,000)	(1,000)	13,000
Change in carrying value of preferred stock warrant liability	(39,000)	(202,000)	(215,000)
Depreciation and amortization	346,000	197,000	1,929,000
Loss on disposal of property and equipment	2,000	7,000	56,000
Noncash interest expense	61,000	588,000	868,000
Changes in operating assets and liabilities:			
Accounts receivable, prepaid expenses and other current assets	(61,000)	(229,000)	(567,000)
Accounts payable	(163,000)	14,000	914,000
Accrued expenses	489,000	(467,000)	2,274,000
Net cash used in operating activities	(21,005,000)	(16,614,000)	(90,652,000)
Cash flows from investing activities:			
Purchases of property and equipment	(180,000)	(7,000)	(2,220,000)
Proceeds from sale of property and equipment	—	—	4,000
Increase in restricted cash	—	—	(117,000)
Net cash used in investing activities	(180,000)	(7,000)	(2,333,000)
Cash flows from financing activities:			
Payments on capital lease	(3,000)	—	(15,000)
Proceeds from sale of common stock	3,000	35,000	93,000
Proceeds from issuance of convertible promissory notes	—	8,824,000	15,824,000
Proceeds from loans payable	10,000,000	—	10,695,000
Payments on loans payable	(376,000)	(3,084,000)	(4,025,000)
Cash paid for debt issuance costs	(4,000)	(373,000)	(432,000)
Proceeds from sale of redeemable convertible preferred stock — net of issuance costs	12,927,000	—	76,333,000
Net cash provided by financing activities	22,547,000	5,402,000	98,473,000
Net increase (decrease) in cash and cash equivalents	1,362,000	(11,219,000)	5,488,000
Cash and cash equivalents — Beginning of period	15,345,000	16,707,000	—
Cash and cash equivalents — End of period	$ 16,707,000	$ 5,488,000	$ 5,488,000
Supplemental disclosures of noncash investing and financing activities:			
Conversion of redeemable convertible preferred stock into common stock	$ —	$ 2,226,000	$ 2,226,000
Conversion of accrued interest and convertible notes payable to Seed Redeemable Convertible Preferred Stock	$ —	$ —	$ 522,000
Conversion of accrued interest and convertible notes payable to Series C Redeemable Convertible Preferred Stock	$ —	$ —	$ 6,676,000
Property and equipment acquired under capital lease	$ —	$ —	$ 15,000
Accretion of redeemable convertible preferred stock to redemption value	$ 73,000	$ —	$ 694,000
Fair value of preferred stock warrants issued in connection with debt	$ 360,000	$ —	$ 1,143,000
Supplemental cash flow information — Interest paid	$ 507,000	$ 664,000	$ 1,293,000

See notes to the 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 Cambridge, Massachusetts. The Company was formed to develop novel, nanotechnology-based therapeutics in the areas of oncology and other diseases. During 2013, the Company formed a wholly-owned subsidiary, Cerulean Pharma Australia Pty Ltd as an Australian-based proprietary limited company. The activity in the subsidiary to date has been insignificant.

Basis of Presentation and Going Concern — The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. Since its date of incorporation, the Company has incurred net losses and negative cash flows from operations, and at December 31, 2013, has an accumulated deficit of approximately $98.4 million and a working capital deficiency of approximately $8.7 million. The Company has financed its operations to date almost exclusively from preferred stock and debt financings. In 2014, the Company raised approximately $8.5 million through the issuance of convertible promissory notes to certain existing investors and a new investor (see Note 18). Management believes that its current cash and cash equivalents with the additional financing received in 2014, are sufficient to fund the Company's operations through June 2014. In addition, the Company is subject to a number of risks common to emerging companies in the life science industry. Principal among these risks are: the Company's need to obtain additional financing necessary to fund future operations; uncertainty of regulatory approval and market acceptance of the Company's products; the Company's compliance with government regulations and approval requirements; uncertainties of the product innovations by the Company's competitors; and the Company's protection of proprietary technology.

The Company will continue to require substantial funds to continue its research and development activities, including pre-clinical studies and clinical trials of its product candidates, and to commence sales and marketing efforts, if the U.S. Food and Drug Administration or other regulatory approvals are obtained. Management's plans in order to meet its short-term and longer term operating cash flow requirements include obtaining additional funding from its current investors and a planned initial public offering ("IPO") of its common stock. The Company confidentially submitted an initial registration statement with the Securities and Exchange Commission to begin the IPO process in January 2014. In February 2014, the Company issued convertible promissory notes to the existing investors totaling $6.0 million and in March 2014, the Company issued a convertible promissory note in the amount of $2.5 million to a new investor (see Note 18). Management is also actively pursuing financial and strategic alternatives, including collaboration agreements with strategic partners.

The uncertainties associated with the Company's ability to (1) obtain additional debt or equity financing on terms that are favorable to the Company, (2) enter into collaborative agreements with strategic partners, and (3) succeed in its future operations, raise substantial doubt about the Company's ability to continue as a going concern. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or amounts of liabilities that might be necessary should the Company be unable to continue its operations. If the Company is not able to obtain the required funding in the near future or is not able to obtain funding on terms that are favorable to the Company, it will have a material adverse effect on its operations and strategic development plan for future growth. If the Company cannot successfully raise additional funding and implement its strategic development plan, then its liquidity, financial condition and business prospects will be materially and adversely affected, and the Company may have to cease operations.

2. SIGNIFICANT ACCOUNTING POLICIES

Use of Estimates — The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of costs and expenses during the reporting period. Significant estimates relied upon in preparing these financial statements include the fair value of common stock, the fair value of preferred stock warrants, recoverability of the Company’s net deferred tax assets, and related valuation allowance and certain accruals. Actual results could differ materially from those estimates.

Principles of Consolidation — The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. All intercompany accounts and transactions have been eliminated.

Unaudited Pro Forma Information — The unaudited pro forma consolidated balance sheet information as of December 31, 2013 reflects the automatic conversion of redeemable convertible stock (see Note 8) and the conversion of convertible notes to shareholders and accrued interest as of December 31, 2013 (see Note 6) into shares of common stock immediately prior to the closing of an initial public offering for a total of 8,366,375 shares of common stock. In addition, the unaudited pro forma consolidated balance sheet information as of December 31, 2013 reflects the conversion of preferred stock warrants into common stock warrants. For purposes of pro forma basic and diluted loss per share attributable to common stockholders, all shares of redeemable convertible preferred stock and convertible notes have been treated as though they had been converted to common stock in all periods in which such shares were outstanding. Accordingly, the pro forma basic and diluted loss per share attributable to common stockholders does not include the effects of the accretion of redeemable convertible preferred stock to redemption value and the interest expense on the convertible notes payable.

Segment Information — Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment.

Cash and Cash Equivalents — Cash equivalents include all highly liquid investments maturing within 90 days from the date of purchase and consist primarily of money market funds.

Concentrations of Credit Risk — Financial instruments that subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. Substantially all of the Company’s cash and cash equivalents are held at one financial institution that management believes to be of high-credit quality. Deposits with this financial institution may exceed the amount of insurance provided on such deposits; however these deposits may be redeemed upon demand and, therefore, bear minimal risk.

Restricted Cash — At December 31, 2012 and 2013, the Company has restricted cash of $117,000 included in other assets representing a letter of credit for the Company’s facility lease that was scheduled to expire in February 2013. The letter of credit is secured by certificates of deposit that renew monthly. The lease was extended through February 2016 and the letter of credit remained intact.

Deferred Issuance Costs — Deferred issuance costs, which primarily consist of direct incremental legal and accounting fees relating to the Company’s planned IPO, are capitalized. The deferred issuance costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. As of December 31, 2013, the Company had capitalized $680,000 of deferred IPO costs, which are included in other current assets on the balance sheet. No amount was deferred as of December 31, 2012.

Property and Equipment — Property and equipment are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Repairs and maintenance costs are expensed as incurred, whereas major improvements are capitalized as additions to property and equipment.

Depreciation is provided using the straight-line method over the following estimated useful lives:

Laboratory equipment	5 years
Computer equipment and purchased software	3 years
Office furniture and equipment	5 years
Leasehold improvements	Lesser of useful life or remaining lease term

Impairment of Long-Lived Assets — Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If this comparison indicates that there is impairment, the amount of impairment is calculated as the difference between the carrying value and fair value. For the years ended December 31, 2012 and 2013, the Company has not recorded an impairment charge for its long-lived assets.

Revenue Recognition — The Company's revenue to date has been insignificant and has been generated from short term research agreements with pharmaceutical companies and federal grants. There have been no multiple element arrangements. Revenue is recognized when four basic criteria are met: (1) persuasive evidence of an arrangement exists, (2) delivery has occurred or services have been rendered, (3) the fee is fixed or determinable, and (4) collectability is reasonably assured. Accordingly the Company has recognized revenue under its agreements as the services were performed.

Research and Development Costs — Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits for full-time research and development employees, an allocation of facilities expenses, overhead expenses, manufacturing process-development and scale-up activities, clinical trial and related clinical manufacturing expenses, fees paid to clinical research organizations, or CROs, and investigative sites, payments to universities under the Company's license agreements and other outside expenses. In the early phases of development, the Company's research and development costs are often devoted to expanding its product platform and are not necessarily allocable to a specific target. Research and development costs are expensed as incurred. Nonrefundable advanced payments, if any, for goods and services used in research and development are recognized as an expense as the related goods are delivered or services are performed.

Preferred Stock Warrant Liability — Freestanding warrants related to shares that are redeemable or contingently redeemable are classified as a liability on the Company's balance sheets. The Company uses the Black-Scholes option-pricing model to estimate the fair value of the warrants. Changes in the fair value of these warrants are recorded in the statements of operations. The Company classifies the liabilities as noncurrent as the settlement of the warrants is not expected within the next twelve months.

Redeemable Convertible Preferred Stock — The Company classifies redeemable convertible preferred stock that is redeemable outside of the Company's control outside of permanent equity. The Company recorded such redeemable preferred stock at fair value upon issuance, net of any issuance costs or discounts, and the carrying value is being increased by periodic accretion to its redemption value. In the absence of retained earnings these accretion charges are recorded against additional paid in capital, if any, and then to accumulated deficit. The Company amortizes the accretion using the interest method.

Stock-Based Compensation — The Company accounts for stock-based awards at fair value, which is measured using the Black-Scholes option-pricing model. The fair value measurement date for employee awards is generally the date of grant. The fair value measurement date for nonemployee awards is generally the date the performance of services is completed. Stock-based compensation costs are recognized as an expense over the requisite service period, which is generally the vesting period, on a straight-line basis for all time-vested awards.

Stock-based awards to nonemployees are remeasured at each reporting date and recognized as services are rendered, generally on a straight-line basis. The Company believes that the fair value of these awards is more reliably measurable than the fair value of the services rendered. Stock-based compensation is classified in the accompanying consolidated statements of operations in the department where the related services are provided.

Net Loss per Share Attributable to Common Stockholders — Basic net loss attributable to common stockholders per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period. During periods where the Company might earn net income, the Company would allocate participating securities a proportional share of net income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the “two-class method”). The Company’s preferred stock participates in any dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods where the Company incurred net loss, the Company allocates no loss to participating securities because they have no contractual obligation to share in the losses of the Company. The Company computes diluted loss per common share after giving consideration to the dilutive effect of stock options, warrants and unvested restricted stock that are outstanding during the period, except where such nonparticipating securities would be antidilutive.

Income Taxes — Deferred income taxes are provided for the temporary differences arising between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes and for operating loss carryforwards and credits. Deferred tax assets and liabilities are recorded using tax rates expected to be in effect in the year in which the differences are expected to reverse. A valuation allowance is provided for any net deferred tax assets for which management believes it is more likely than not that the net deferred tax assets will not be realized.

The Company provides reserves for potential payment of tax to various tax authorities related to uncertain tax positions. The tax benefits recorded are based on a determination of whether and how much of a tax benefit taken by the Company in its filings or positions is “more likely than not” to be realized following resolution of any uncertainty related to the tax benefit, assuming the matter in question will be raised by the tax authorities. Potential interest and penalties associated with such uncertain tax positions are recorded as a component of income tax expense. At December 31, 2012 and 2013, the Company has not identified any significant uncertain tax positions.

Guarantees and Indemnification — As permitted under Delaware law, the Company indemnifies its officers, directors, and employees for certain events or occurrences while the officer or director is, or was serving at the Company’s request in such a capacity. The term of the indemnification is for the officer’s or director’s lifetime.

Subsequent Events — The Company has evaluated subsequent events through March 7, 2014, the date on which the accompanying financial statements were originally issued. In connection with the reverse stock split described in Note 18, the Company evaluated subsequent events through March 31, 2014, the date on which the revised accompanying financial statements were issued.

3. NET LOSS PER SHARE ATTRIBUTABLE TO COMMON STOCKHOLDERS

The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company:

	Years Ended December 31,	
	2012	2013
Net loss	$ (22,101,000)	$ (17,143,000)
Accretion of preferred stock issuance costs to redemption value	(73,000)	—
Net loss attributable to common stockholders — basic and diluted	$ (22,174,000)	$ (17,143,000)
Weighted-average number of common shares — basic and diluted	609,344	684,330
Net loss per share attributable to common stockholders — basic and diluted	$ (36.39)	$ (25.05)

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

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

	As of December 31,	
	2012	2013
Options to purchase common stock	1,046,178	1,062,694
Warrants to purchase redeemable convertible preferred stock	128,672	128,672
Redeemable convertible preferred stock	6,992,694	6,826,019
Convertible notes payable	—	754,785

The unaudited pro forma basic and diluted loss per share attributable to common stockholders for the year ended December 31, 2013 give effect to the automatic conversion of all shares of redeemable convertible preferred stock upon an initial public offering by treating all shares of redeemable convertible preferred stock as if they had been converted to common stock in all periods in which such shares were outstanding. In addition the pro forma basic and diluted loss per share attributable to common stockholders give effect to the automatic conversion of the convertible notes (see Note 6) using a per share price of $12.00 the mid point of the estimated price range in the contemplated IPO. In the event a qualified financing including the contemplated IPO, is not completed prior to August 15, 2014 when the convertible notes may be converted into Series D Preferred Stock on demand by the noteholders. Accordingly, the pro forma basic and diluted loss per share attributable to common stockholders do not include effects of the accretion of redeemable convertible preferred stock to redemption value and the interest expense on the convertible notes payable. Shares to be sold in the offering are excluded from the unaudited pro forma basic and diluted loss per share attributable to common stockholders calculations. As the Company incurred a net loss for the year ended December 31, 2013, there is no income allocation required under the two-class method or dilution attributed to pro forma weighted-average shares outstanding in the calculation of pro forma diluted loss per share attributable to common stockholders.

Unaudited pro forma basic and diluted loss per share attributable to common stockholders are computed as follows:

Pro forma loss per share — basic and diluted	**Year Ended December 31, 2013**
Numerator:	
Net loss attributable to common stockholders — basic and diluted	$ (17,143,000)
Add: Accretion of preferred stock issuance costs to redemption value	—
Add: Interest expense on convertible notes payable	234,000
Net loss attributable to common stockholders — basic and diluted	$ (16,909,000)
Denominator:	
Weighted-average number of shares outstanding — basic and diluted	684,330
Add: adjustment to reflect assumed effect of conversion of redeemable convertible preferred stock and convertible notes payable	7,198,874
Pro forma weighted-average number of shares outstanding — basic and diluted	7,883,204
Pro forma basic net loss per share — basic and diluted	$ (2.14)

4. PROPERTY AND EQUIPMENT

Property and equipment, consist of the following:

	December 31,	
	2012	**2013**
Laboratory equipment	$ 1,417,000	$ 1,246,000
Computer equipment and purchased software	193,000	183,000
Office furniture and equipment	257,000	257,000
Leasehold improvements	91,000	91,000
	1,958,000	1,777,000
Less accumulated depreciation and amortization	(1,516,000)	(1,532,000)
	$ 442,000	$ 245,000

Depreciation and amortization expense for the years ended December 31, 2012 and 2013 was $346,000 and $197,000, respectively.

5. ACCRUED EXPENSES

Accrued expenses consist of the following:

	As of December 31,	
	2012	**2013**
Accrued expenses	$ 316,000	$ 613,000
Accrued clinical trial costs	989,000	610,000
Accrued contract manufacturing expenses	974,000	433,000
Accrued compensation and benefits	462,000	618,000
Total accrued expenses	$2,741,000	$2,274,000

6. CONVERTIBLE NOTES PAYABLE TO SHAREHOLDERS

In May 2010 and September 2010, the Company issued one-year convertible notes payable in the amounts of $5,000,000 and $1,500,000, respectively, to existing investors, with a stated interest rate of 7%. In November 2010, the principal and accrued interest of $176,000 were converted into 9,021,175 shares of Series C Preferred Stock at $0.74 per share (see Note 8). The Company also provided for the issuance of seven-year warrants to purchase Series C Preferred Stock with the notes. The issuance of the warrants was contingent upon the conversion of the notes to Series C Preferred Stock. The number of shares included in the warrants was determined by dividing 10% of the note principal converted to Series C Preferred Stock by the Series C Preferred Stock per share issue price. Concurrent with the conversion of the notes, warrants to purchase 878,370 shares of Series C Preferred Stock at $0.74 per share became exercisable. The Company estimated the fair value of the warrants on the issue date to be $474,000 using the Black-Scholes option-pricing model with the following assumptions: volatility of 80%, contractual term of seven years, risk-free interest rate of 1.85%, and no dividend yield. As of December 31, 2012 and 2013, the estimated fair value of the warrants was $500,000 and $386,000, respectively, estimated using the Black-Scholes option-pricing model with the following assumptions: volatility of 86% and 65%, remaining contractual term of 5 and 4 years, risk-free interest rate of 1.13% and 2.29%, respectively, and no expected dividends. These warrants are classified as a liability in the accompanying balance sheets. The adjustments to the Series C Preferred Stock warrant liability recorded as other income (expense) in the years ended December 31, 2012 and 2013, were $18,000 and $114,000, respectively.

On August 15, 2013, the Company issued convertible promissory notes in the amount of $8,824,000, to existing investors, with a stated interest rate of 7%. The notes are payable on demand by the investors on or after August 15, 2014. Principal and unpaid accrued interest due under these notes will automatically be converted into the Company’s capital stock at the closing of the Company’s next qualified financing or upon a qualified initial public offering, based on a conversion price equal to the price per share paid by other investors in the financing. If the financing does not occur on or before August 15, 2014, the principal and unpaid accrued interest can be converted by the investors into shares of the Company’s Series D Convertible Preferred Stock at a price of $0.83 per share (subject to adjustment). No additional financing has occurred to date.

7. LOAN AGREEMENTS

In August 2008, the Company entered into a Loan and Security Agreement (the “Loan Agreement”) with a bank to borrow up to $1,500,000 in one or more advances to finance certain equipment purchases made by the Company through May 31, 2009. In September 2008, the Company received its only advance totaling $695,000 and issued a note payable to the bank. No additional advances were made. The note was payable over a 48-month period in equal principal payments, plus interest on the outstanding balance, fixed at the 8.75%. The note was secured by a security interest in the specific equipment financed. In September 2012, the Company paid the remaining balance in accordance with the original repayment schedule.

In connection with the Loan Agreement, the Company issued the bank a warrant to purchase 15,000 shares of the Company’s Series B Preferred Stock at an exercise price of $2.00 per share. The warrant was immediately exercisable and expires 10 years from the date of grant (August 2018). The value of the warrant was recorded as a discount to the note payable and was amortized to interest expense using the effective interest method over the 48-month repayment term. The Company estimated the fair value of the warrant on the grant date to be $25,000 using the Black-Scholes option-pricing model with the following assumptions: volatility of 79%, contractual term of 10 years, risk-free interest rate of 3.89%, and no dividend yield. As of December 31, 2012 and 2013, the estimated fair value of the warrant was $7,000 and $4,000, respectively, estimated using the Black-Scholes option-pricing model with the following assumptions: volatility of 84% and 64%, remaining contractual term of 6 and 5 years, risk-free interest rate of 1.72% and 2.90%, respectively, and no expected dividends. The warrant is classified as a liability in the accompanying balance sheets. The adjustments to the Series B Preferred Stock warrant liability recorded as other income in the years ended December 31, 2012 was immaterial, and $3,000 for the year ended December 31, 2013.

In December 2011, the Company entered into a loan and security agreement with Lighthouse Capital Partners VI, L.P. ("Lighthouse Capital") to borrow up to $10,000,000 in one or more advances by December 31, 2012. Debt proceeds are available to the Company to fund research and development activities and other general corporate purposes. The Company granted Lighthouse Capital a first priority security interest in all unsecured present and future assets, other than intellectual property, and the Company entered into a negative pledge agreement with the lender, whereby the Company agrees not to grant a security interest in or encumber any of the Company's intellectual property. The Company also has restrictions on its ability to obtain additional debt that is not permitted under the agreement. No advances were made under this loan and security agreement in 2011. In both March 2012 and August 2012, the Company borrowed $5,000,000 under the loan and security agreement, for a total of $10,000,000. This amount is being repaid over 36 months beginning on December 1, 2012, at an interest rate of 8.25%.

In addition, the Company is required to make an additional interest payment in the amount of $600,000 at the end of the loan term. The amount is being accrued over the loan term as interest expense. The amounts accrued as of December 31, 2012 and December 31, 2013 total $37,000 and $391,000, respectively and are included as non-current accrued interest expense in the accompanying balance sheets. The minimum future principal payments are as follows:

Years Ending December 31,	
2014	$ 3,349,000
2015	3,321,000
Total	6,670,000
Unamortized discount relating to warrants	(412,000)
Total	6,258,000
Less current portion	(3,134,000)
Long-term portion	$ 3,124,000

In connection with the loan and security agreement with Lighthouse Capital, the Company issued the lender a warrant to purchase a maximum of 963,856 shares of the Company's Series D Preferred Stock, at an exercise price of $0.83 per share. The warrant was immediately exercisable for 421,687 shares at the date of issue and expires 10 years from the date of issue (December 2021). The exercisable shares increased in March 2012 and August 2012 as the Company borrowed under the loan and security agreement. At December 31, 2012, 963,856 shares were exercisable. The fair value of the warrant was estimated on the date of issue for the exercisable shares at that date and the fair value of each increment was estimated on the date the shares became exercisable, using the Black-Scholes option-pricing model. The Company estimated the fair value of the warrant for shares exercisable on the issue date in December 2011 and incremental shares exercisable in March 2012 and August 2012 to be $284,000, $182,000 and $178,000, respectively. The following table shows the Black-Scholes assumptions used to value the preferred stock warrants in connection with the loan and security agreement on the respective dates:

	Series D Preferred Stock Warrants		
	December 2011	March 2012	August 2012
Contractual life	10 years	9.69 years	9.29 years
Volatility rate	80%	80%	80%
Risk-free interest rate	1.98%	2.17%	1.68%
Expected dividends	—	—	—

The value of the warrant is recorded as a discount to the note payable and is being amortized to interest expense using the effective interest method over the 36-month repayment term.

As of December 31, 2012 and 2013, the estimated fair value of the warrants was $623,000 and $538,000, respectively, estimated using the Black-Scholes option-pricing model with the following assumptions: volatility of 79% and 64%, remaining contractual term of 9 and 8 years, risk-free interest rate of 1.72% and 2.90%, respectively, and no expected dividends. The warrant is classified as a liability in the accompanying balance sheets. The adjustment to the Series D Preferred Stock warrant liability recorded as other income in the year ended December 31, 2012 was $21,000 and $85,000 in the year ended December 31, 2013.

8. REDEEMABLE CONVERTIBLE PREFERRED STOCK

The following is a summary of the Company's convertible redeemable preferred stock.

Preferred stock consisted of the following as of December 31, 2012:

	Preferred Shares Authorized	Issuance Date	Preferred Shares Issued and Outstanding	Redemption Value/Liquidation Preference	Carrying Value
Seed	2,500,000	December 2006	2,500,000	$ 2,000,000	$ 2,000,000
Series A	9,307,692	May 2007	9,307,692	12,100,000	12,100,000
Series B	4,077,500	December 2007	4,062,500	8,125,000	8,125,000
Series B-1	5,000,000	July 2009	5,000,000	10,000,000	10,000,000
Series C	33,310,787	November 2010 and June 2011	32,432,417	24,000,000	23,526,000
Series D	34,698,793	December 2011 and November 2012	33,733,937	28,000,000	28,000,000
	88,894,772		87,037,546	$ 84,225,000	$ 83,751,000

Preferred stock consisted of the following as of December 31, 2013:

	Preferred Shares Authorized	Issuance Date	Preferred Shares Issued and Outstanding	Redemption Value /Liquidation Preference	Carrying Value
Seed	2,500,000	December 2006	2,500,000	$ 2,000,000	$ 2,000,000
Series A	9,307,692	May 2007	9,307,692	12,100,000	12,100,000
Series B	4,077,500	December 2007	3,562,500	7,125,000	7,125,000
Series B-1	5,000,000	July 2009	4,842,500	9,685,000	9,685,000
Series C	33,310,787	November 2010 and June 2011	31,836,392	23,559,000	23,094,000
Series D	34,698,793	December 2011 and November 2012	33,158,272	27,521,000	27,521,000
	88,894,772		85,207,356	$ 81,990,000	$ 81,525,000

In December 2005, the Company entered into an agreement with a potential investor for a one-year convertible note payable in the amount of $500,000, with a stated interest rate of 4.5%. In December 2006, the Company issued an aggregate of 2,500,000 shares of Seed Redeemable Convertible Preferred Stock ("Seed Preferred") at an original issuance price of $0.80 per share for gross proceeds of $1,500,000 and the conversion of $500,000 of convertible promissory notes and $22,000 of accrued interest and incurred issuance costs of $83,000.

In May 2007, the Company sold 9,307,692 shares of Series A Redeemable Convertible Preferred Stock ("Series A Preferred") at an original issuance price of $1.30 per share for gross proceeds of $12,100,000, and incurred issuance costs of $56,000.

In December 2007, the Company sold 4,062,500 shares of Series B Redeemable Convertible Preferred Stock ("Series B Preferred") at an original issuance price of $2.00 per share for gross proceeds of $8,125,000 and incurred issuance costs of $45,000.

In July 2009, the Company sold 5,000,000 shares of Series B-1 Redeemable Convertible Preferred Stock ("Series B-1 Preferred") at an original issuance price of $2.00 per share for gross proceeds of $10,000,000 and incurred issuance costs of $75,000.

In November 2010, the Company issued an aggregate of 22,297,289 shares of Series C Preferred Stock ("Series C Preferred") at an original issuance price of $0.74 per share for gross proceeds of $10,000,000 and the conversion of the $6,500,000 of convertible promissory notes and $176,000 of accrued interest (see Note 6) and incurred issuance costs of $264,000.

In June 2011, the Company sold 10,135,128 shares of Series C Preferred at an issuance price of $0.74 per share for gross proceeds of $7,500,000 and incurred issuance costs of $22,000.

In December 2011, the Company sold 18,072,287 shares of Series D Redeemable Convertible Preferred Stock ("Series D Preferred") at an original issuance price of $0.83 per share for gross proceeds of $15,000,000 and incurred issuance costs of $76,000.

In November 2012, the Company sold 15,662,650 shares of Series D Preferred Stock at an original issuance price of $0.83 per share for gross proceeds of $13,000,000 and incurred issuance costs of $73,000.

In July 2013, the Company converted 500,000, 157,500, 596,025, and 576,665 shares of Series B Preferred, Series B-1 Preferred, Series C Preferred and Series D Preferred stock, respectively, into 166,675 shares of the Company's common stock.

Warrants — The Company's outstanding warrants are detailed in the table below:

		Fair value at December 31,	
Warrants to Purchase	**Number of Shares**	**2012**	**2013**
Series B Preferred Stock	15,000	$ 7,000	$ 4,000
Series C Preferred Stock	878,370	500,000	386,000
Series D Preferred Stock	963,856	623,000	538,000
	1,857,226	$ 1,130,000	$ 928,000

The Seed Preferred, Series A Preferred, Series B Preferred, Series B-1 Preferred, Series C Preferred, and Series D Preferred (collectively, "Preferred Stock") have the following rights and privileges:

Voting — The holders of the Preferred Stock are entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote, except with respect to matters on which Delaware General Corporation Law requires that a vote will be by a separate class. Each preferred stockholder is entitled to the number of votes equal to the number of shares of common stock into which each preferred share then held by such stockholder is convertible at the time of such vote. The holders of the Seed Preferred, the Series A Preferred, the Series C Preferred, and the Series D Preferred have voting preferences in that they each have the exclusive right to elect one director to the Company's Board of Directors ("Preferred Directors"). The consent of the Preferred Directors is required for the Company to effect certain transactions.

Dividends — The holders of Series A Preferred, Series B Preferred, Series B-1 Preferred, Series C Preferred, and Series D Preferred stock are entitled to receive noncumulative dividends at the annual rate of 8% on the respective original issue price, as defined, when and if declared by the Board of Directors. Additionally, in the event that a dividend is declared for the holders of common stock, the holders of the Preferred Stock are entitled to the amount of dividends on an as-converted basis. No dividends have been declared since the Company's incorporation.

Liquidation Preference — In the event of any liquidation, dissolution, change of control, as defined, or winding up of the affairs of the Company, the holders of the then-outstanding Preferred Stock shall receive the respective original issue price, plus all declared but unpaid dividends, payable in preference and priority to any payments made to the holders of the then-outstanding common stock. After payment to the holders of the Preferred Stock of the preferential amounts so payable to them, any remaining assets of the Company shall be distributed to the holders of the common stock and the Preferred Stock ratably in proportion to the number of shares of common stock they then hold, determined for this purpose as if each share of Preferred Stock had been converted voluntarily into common stock at the then-applicable conversion price immediately prior to the liquidation event, provided that the aggregate of all liquidation payments to Preferred Stockholders will not exceed two times the original issue price, for each share of Preferred Stock. Any remaining assets of the Company shall be distributed to the holders of the common stock ratably in proportion to the number of shares of common stock they then hold. If the assets or surplus funds to be distributed to the holders of the Preferred Stock are insufficient to permit the payment to such holders of their full preferential amount, the assets and surplus funds legally available for distribution shall be distributed ratably among the holders of the Preferred Stock in proportion to the full preferential amount each such holder is otherwise entitled to receive.

Conversion — Each share of Preferred Stock, at the option of the holder, is convertible into that number of the fully paid shares of common stock as determined by dividing the sum of the original issuance price, plus any declared but unpaid dividends by the conversion price in effect at the time of conversion. The initial conversion price is the respective original issue price, subject to adjustment in accordance with the antidilution provisions of each series. Conversion is automatic immediately upon the closing of a firm commitment underwritten public offering with an offering price of at least $2.50 per share, and resulting in at least $30,000,000 of gross proceeds to the Company, pursuant to an effective registration statement under the Securities Exchange Act of 1933, as amended, provided such offering has been approved by the Company's Board of Directors, including the Preferred Directors as defined above, or upon the written consent of at least 58% of the Preferred Stock outstanding at that time. As of December 31, 2013, the conversion rate for the Seed Preferred, Series A, Series B, Series B-1, Series C and Series D to common stock is on a basis of 1 to 0.073, 1 to 0.092, 1 to 0.113, 1 to 0.186, 1 to 0.069, 1 to 0.069, respectively, immediately prior to the closing of an initial public offering.

Redemption — With a vote by holders of at least 58% of the Preferred Stock voting together as a single class, each holder of the Preferred Stock has the right to cause the Company, on or after the fifth anniversary of the Series D original issue date (December 2, 2016), to redeem the Preferred Stock, at a price equal to the original issuance price, plus all declared but unpaid dividends, in three annual installments.

9. STOCKHOLDERS' DEFICIT

Common Stock — During 2006, the Company issued an aggregate of 516,958 shares of common stock to the founders of the Company for aggregate consideration of $1,000, the then deemed fair value of the common stock.

In April 2007, the Company entered into consulting agreements with two members of its Board of Directors, and as compensation for their services issued a total of 31,016 shares of common stock to the directors at par value of $0.0001, for total consideration of $45. The shares were subject to vesting restrictions that lapsed on a straight-line basis over 48 months, beginning in January 2007 and becoming fully vested in 2010. The Company had the right to repurchase the unvested shares at the original purchase price, if the relationship between the Company and the shareholder was terminated during the vesting period. All shares of common stock that were subject to repurchase restrictions had the same rights and privileges as unrestricted shares of common stock and were presented as outstanding as the restrictions lapsed. The restricted common stock issued to nonemployees was subject to remeasurement, and the Company recorded the value at the time services were provided and the shares vested.

In December 2006, the Company issued an aggregate of 36,270 shares of common stock to the Massachusetts Institute of Technology (MIT) and certain individuals affiliated with MIT, pursuant to a technology license agreement ("MIT License"). The deemed fair value of the shares of common stock of $142,000 was recorded as research and development expense in 2006. In March 2007 and May 2007, as a result of certain antidilution provisions in the MIT License, the Company issued an aggregate of 12,897 shares of common stock to MIT at a deemed fair value of $60,000, which was recorded as research and development expense in 2007. The anti-dilution provisions of the license provided that the Company issue additional shares such that the MIT holders' ownership of the outstanding common stock did not fall below 5% on a fully diluted basis until a total of $5,000,000 in cash had been raised by the Company with the sale of the Company's capital stock. The Company's antidilution obligations associated with the MIT License were satisfied in May 2007, as a result of the Series A Preferred Stock financing, and no additional shares of common stock will be issued under the MIT License.

Reserved Shares of Common Stock — The Company has reserved the following number of shares of common stock at December 31, 2013, for the potential conversion of designated Preferred Stock and the exercise of the stock options summarized below:

Seed Preferred Stock	181,399
Series A Preferred Stock	859,842
Series B Preferred Stock	404,254
Series B-1 Preferred Stock	902,151
Series C Preferred Stock	2,255,015
Series D Preferred Stock	2,352,030
Common Stock options	1,201,770
Total	8,156,461

10. STOCK OPTION PLAN

The Company's 2007 Incentive Stock Plan (the "Plan") provides for the grant of qualified incentive stock options and nonqualified stock options or other awards to the Company's employees, officers, directors, advisors, and outside consultants to purchase up to an aggregate of 1,254,532 shares of the Company's common stock, as amended in February 2013. The stock options generally vest over a four-year period and expire 10 years from the date of grant. Certain options provide for accelerated vesting if there is a change in control, as defined in the Plan. The Company generally issues previously unissued shares of common stock for the exercise of stock options. At December 31, 2012, there were 74,902 shares available for future grant under the Plan. As of December 31, 2013 there were 139,076 shares available for future grant under the Plan.

The Company has recorded stock-based compensation expense of $529,000 and $622,000 during the years ended December 31, 2012 and 2013, respectively, which is based on the number of awards ultimately expected to vest. As of December 31, 2012 and December 31, 2013, there was $1,069,000 and $609,000, respectively, of unrecognized compensation cost related to unvested stock-based compensation arrangements granted under the Plan, which is expected to be recognized over a weighted-average period of 2.85 and 2.11 years at December 31, 2012 and December 31, 2013.

Stock-based compensation expense recorded as research and development and general and administrative expenses is as follows:

	As of December 31,	
	2012	2013
Research and development	$ 187,000	$ 284,000
General and administrative	342,000	338,000
Total	$ 529,000	$ 622,000

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, 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.

In determining the exercise prices for options granted, the Company's Board of Directors has considered the fair value of the common stock as of the measurement date. The fair value of the common stock has been determined by the Board of Directors at each award grant date based upon a variety of factors, including the results obtained from a common stock valuation, the Company's financial position and historical financial performance, the status of technological developments within the Company's products, the composition and ability of the current research and management team, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's-length sales of the Company's capital stock (including redeemable convertible preferred stock), the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event, among others.

The assumptions used in the Black-Scholes option-pricing model for stock options granted to employees during the years ended December 31, 2012 and 2013 are as follows:

	December 31,	
	2012	2013
Expected life	6 years	6 years
Risk-free interest rate	0.83%-1.12%	1.09%-1.92%
Expected volatility	77%-79%	59%-79%
Expected dividend rate	— %	— %

A summary of stock option activity for employee and nonemployee awards under the Plan during the year ended December 31, 2013 is presented below:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value
Outstanding — January 1, 2013	1,046,178	$ 3.95	8.3	$ 274,000
Granted	112,515	$ 4.03		
Exercised	(8,911)	$ 4.01		
Forfeited	(87,088)	$ 3.63		
Outstanding — December 31, 2013	1,062,694	$ 3.98	7.2	$7,028,000
Options expected to vest — December 31, 2013	434,064	$ 3.77	8.5	$2,941,000
Options exercisable — December 31, 2013	606,695	$ 4.06	6.2	$3,939,000

The total intrinsic value of stock options exercised in the years ended December 31, 2012 and 2013 and for the period November 28, 2005 (date of incorporation) to December 31, 2013 was $0, $15,000, and $25,000, respectively.

The weighted-average per share grant date fair value of options granted during 2012 and 2013 was $2.61 and $2.90, respectively.

The Company did not grant any nonemployee stock option grants in 2012 or in 2013, except for the performance award grant to the board chairman discussed below. In 2011, the Company granted options for 53,145 shares of common stock to nonemployees with an initial fair value of $161,000. The Company has recorded stock-based compensation expense related to nonemployee awards of $39,000, and $85,000 in 2012 and 2013, respectively. The compensation expense related to the nonemployee awards is included in the total stock-based compensation each year and is subject to re-measurement until the options vest. The Black-Scholes assumptions used to estimate fair value at December 31, 2012 and for December 31, 2013 were as follows: risk-free rate of 0.99% to 2.05% and 0.22% to 3.01%, estimated volatility of 76% to 79% and 55% to 79%, remaining contractual life of 6 years and no expected dividends, respectively.

The Company has granted stock options to purchase up to 206,239 shares of common stock to two of the Company’s officers and the board of directors chairman for non-board related services. The vesting of these awards is contingent upon the Company’s stock price upon a change of control or following the time when the Company’s common stock is registered under the Securities Exchange Act of 1934, as amended, and is quoted, listed or traded on an over-the-counter market or national securities exchange. A portion of the awards also vest upon the achievement of business milestones as defined within the stock option agreement. Compensation expense for the awards will be recorded if and when vesting occurs.

11. FAIR VALUE MEASUREMENTS

The Company’s financial instruments consist of cash equivalents, accounts payable, accrued expenses, debt obligations, and preferred stock warrants. 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 the fair value based on the short term nature of the debt and that the debt bears interest at the prevailing market rate for instruments with similar characteristics. Included in cash and cash equivalents as of December 31, 2012 and 2013, are money market fund investments of $16,681,000 and $5,233,000, respectively, which are reported at fair value.

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 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 December 31, 2012 and 2013, is as follows:

		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)
December 31, 2012				
Money market funds	$16,681,000	$ —	$16,681,000	$ —
Preferred stock warrant liability	1,130,000	—	—	1,130,000
December 31, 2013				
Money market funds	$ 5,233,000	$ —	$ 5,233,000	$ —
Preferred stock warrant liability	928,000	—	—	928,000

The convertible notes payable and loan agreements 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.

For the years ended December 31, 2012 and 2013, there have been no transfers between levels.

The reconciliation of the Company's liabilities measured at fair value on a recurring basis using unobservable inputs (Level 3) is as follows:

	Preferred Stock Warrant			
	Series B	Series C	Series D	Total
Balance — January 1, 2012	$ 7,000	$ 518,000	$284,000	$ 809,000
New warrants issued during the year			360,000	360,000
Decrease in fair value recorded in other income	—	(18,000)	(21,000)	(39,000)
Balance — December 31, 2012	7,000	500,000	623,000	1,130,000
Decrease in fair value recorded in other income	(3,000)	(114,000)	(85,000)	(202,000)
Balance — December 31, 2013	$ 4,000	$ 386,000	$538,000	$ 928,000

The Company's warrants were valued using the Black-Scholes option-pricing model (see Notes 6 and 7).

The preferred stock warrant liability will increase or decrease each period based on the fluctuations of the fair value of the underlying preferred security.

12. INCOME TAXES

Significant components of the Company's deferred taxes at December 31, 2012 and 2013 are as follows:

	2012	2013
Net operating loss carryforwards	$ 26,892,000	$ 25,696,000
Research and development credit carryforwards	1,267,000	1,525,000
Capitalized costs	2,741,000	3,067,000
Capitalized research and development costs	—	6,992,000
Other	522,000	220,000
Total deferred tax assets	31,422,000	37,500,000
Valuation allowance	(31,422,000)	(37,500,000)
Net deferred tax assets	$ —	$ —

The Company has provided a valuation allowance for the full amount of deferred tax assets as the realization of the deferred tax assets is not determined to be more-likely-than-not. The valuation allowance increased in 2012 and 2013 by approximately $7,603,000 and $6,078,000, respectively, due to the increase in the deferred tax assets by the same amount.

At December 31, 2013, the Company has approximately $66,807,000 of federal and $54,189,000 of state net operating loss carryforwards that expire at various dates through 2033. At December 31, 2013, the Company has approximately $1,026,000 of federal and $757,000 of state research and development credit carryforwards that expire at various dates through 2033 for federal credits and 2028 for state credits.

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. The future realization of the net operating loss carryforwards may also be limited by the change of ownership rules of the Internal Revenue Service under Section 382 of the Internal Revenue Code. If substantial changes in ownership should occur, there could be annual limitations on the amount of carryforwards that can be realized in future periods.

The Company files income tax returns in the United States and the Commonwealth of Massachusetts. The tax years 2005 through 2013 remain open to examination by these taxing jurisdictions, as carryforwards attributes generated in past years may be adjusted in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years. The Company does not believe material uncertain tax positions have arisen to date.

13. COMMITMENTS

Facility Lease — On November 1, 2009, the Company entered into a noncancelable operating lease with a third party for office and laboratory space that was scheduled to expire in February 2013, subject to a three-year renewal option. The lease agreement includes base rent escalation over the initial term, therefore, the Company is amortizing the cost of the lease on a straight-line basis over the lease term and the resulting deferred liability recorded in other liabilities as of December 31, 2012 and 2013 was $14,000 and $12,000, respectively. Rent expense under this lease was $517,000 and $598,000 for the years ended December 31, 2012 and 2013, respectively. The lease requires the Company to share in prorated expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, not included in the future minimum obligations listed below. In June 2012, the Company exercised its renewal option extending the lease through February 2016.

Future minimum lease payments, including the three-year extension, under the noncancelable operating lease are as follows:

Years Ending December 31,	Operating Leases
2014	610,000
2015	624,000
2016	104,000
Total	$ 1,338,000

14. LICENSING AGREEMENTS

Massachusetts Institute of Technology License — The Company's license agreement with the Massachusetts Institute of Technology ("MIT"), as amended, requires the Company pay MIT nonrefundable annual license maintenance fees that increase each year beginning in 2015 through 2020 and remain constant thereafter. The annual license fee is not material in any individual year. In addition, the Company may be required to pay milestone payments and/or product royalties in the event future partner collaborations or product sales incorporate technology covered by this license agreement. In connection with this agreement, the Company recorded research and development expense for annual maintenance fees of $10,000 each in the years ended December 31, 2012 and 2013, respectively.

Calando License — The Company has a product license agreement and a platform license agreement with Calando Pharmaceuticals, Inc. ("Calando"). Under the product license agreement, the Company may be required to pay Calando up to $32.8 million upon the achievement of specified regulatory and commercial milestones and pay tiered royalty payment ranging from low-to mid-single digits on commercial sales.

Under the platform license agreement, the Company will be required to pay Calando a $250,000 clinical development milestone upon initiation of a Phase 1 clinical trial. In addition, the Company may be required to pay Calando up to $17.8 million upon the achievement of specified regulatory and commercial milestones and pay royalty payments ranging from low-to mid-single digits on commercial sales.

There have been no milestones achieved or commercial sales related to either of the Calando license agreements.

SUNY License — The Company is party to a license agreement with The Research Foundation of State University of New York ("SUNY") for certain intellectual property. The agreement as amended requires the Company to pay nonrefundable annual license maintenance fees each year until the date of first commercial sale of a licensed product pursuant to the license agreement, as amended. The annual license fee is not material in any individual year. In the event of future partner collaborations or product sales incorporating technology covered by this license agreement, the Company may be required to pay milestone payments and/or product royalties. In connection with this agreement, the Company recorded research and development expense of $10,000 and $25,000 for the years ended December 31, 2012 and 2013, respectively.

15. RETIREMENT PLANS

The Company has a 401(k) retirement and profit-sharing plan (the "401(k) Plan") covering all qualified employees. The 401(k) Plan allows each participant to contribute a portion of their base wages up to an amount not to exceed an annual statutory maximum. Effective January 1, 2010, the Company adopted a Safe Harbor Plan that provides a Company match up to 4% of salary. The Company contributed a match of $165,000 and $145,000 to the 401(k) Plan for the years ended December 31, 2012 and 2013, respectively.

16. RELATED PARTY TRANSACTIONS

In April 2013, the Company entered into a laboratory, equipment sharing, services and license agreement with an entity affiliated with one of the Company's directors. Fees recorded offsetting research and development expenses under this agreement and paid in the year ended December 31, 2013, were $84,000.

In August 2013 and February 2014, the Company issued convertible promissory notes to existing investors, as described in Notes 6 and 18.

17. REVENUE

The Company entered into a material transfer agreement in February 2012 with a biopharmaceutical company and amended the agreement in March 2012. The terms of the agreement provided revenue in exchange for conducting research using the Company's proprietary technology and the pharmaceutical company's proprietary compounds. The Company received $625,000 under this agreement and recognized this amount as revenue during 2012, the period when the research work was performed and all deliverables were completed.

In October 2013, the Company entered into a material transfer agreement with another biopharmaceutical company to conduct feasibility studies using the Company's proprietary technology. The Company recognized revenue of $6,000 for the year ended December 31, 2013 in connection with this material transfer agreement.

18. SUBSEQUENT EVENTS

In 2014, the Company issued convertible promissory notes in the aggregate amount of $6,000,000 to existing investors and $2,500,000 to a new investor. All the notes have a stated interest rate of 7%, and are payable within 30 days of written demand by the investors after February 26, 2015. Principal and unpaid accrued interest due under these notes will automatically be converted into the Company's capital stock at the closing of the Company's next qualified financing or upon a qualified initial public offering, based on a conversion price equal to 77.5% of the price per share paid by other investors in the financing. If the notes convert upon the closing of the Company's next qualified financing or a qualified initial public offering, the Company will record a charge equal to the difference between the fair value of the shares into which the notes convert and the carrying amount of the notes. If the financing does not occur on or before February 26, 2015, the principal and unpaid accrued interest can be converted at the election of the investors into shares of the Company's Series D Convertible Preferred Stock at a price of $0.83 per share (subject to adjustment).

In connection with preparing for the public offering of its common stock, the Company's Board of Directors and stockholders approved a reverse stock split of the Company's common stock on a 1 for 14.5074 basis. The reverse stock split became effective on March 31, 2014. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

* * * * * *

CERULEAN

5,000,000 SHARES OF COMMON STOCK

Leerink Partners

Canaccord Genuity **JMP Securities** **Wedbush PacGrow Life Sciences**

Until , 2014 (25 days after commencement of this offering), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Part II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the Securities and Exchange Commission registration fee, the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee and the NASDAQ Global Market listing fee.

	Amount
Securities and Exchange Commission registration fee	$ 9,628
FINRA filing fee	11,713
NASDAQ Global Stock Market listing fee	125,000
Accountants' fees and expenses	1,125,000
Legal fees and expenses	1,340,000
Blue Sky fees and expenses	25,000
Transfer Agent's fees and expenses	5,000
Printing and engraving expenses	185,000
Miscellaneous	14,659
Total expenses	$ 2,841,000

Item 14. Indemnification of Directors and Officers.

Section 102 of the General Corporation Law of the State of Delaware permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation provides that no director of the Registrant shall be personally liable to it or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation, or a person serving at the request of the corporation for another corporation, partnership, joint venture, trust or other enterprise in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he was or is a party or is threatened to be made a party to any threatened, ending or completed action, suit or proceeding by reason of such position, if such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Upon completion of this offering, our certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an “Indemnitee”), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our certificate of incorporation provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys’ fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys’ fees) actually and reasonably incurred in connection therewith. Expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with each of our directors and officers. These indemnification agreements may require us, among other things, to indemnify our directors and officers for some expenses, including attorneys’ fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of our directors or officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

We maintain a general liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended (the “Securities Act”), against certain liabilities.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of our common stock, shares of our preferred stock, warrants to purchase shares of our preferred stock and promissory notes issued, and stock options and restricted stock awards granted, by us within the past three years that were not registered under the Securities Act of 1933, as amended, or the Securities Act. Also included is the consideration, if any, received by us for such shares and options and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of securities

In February and March 2014, we issued convertible promissory notes in an aggregate amount of $8.5 million to 16 investors.

In August 2013, we issued convertible promissory notes in an aggregate principal amount of $8.8 million to 14 investors.

In November 2012, we issued and sold 15,662,650 shares of our Series D preferred stock to 16 investors, at a price per share of $0.83, for an aggregate purchase price of $13.0 million.

In December 2011, we issued and sold 18,072,287 shares of our Series D preferred stock to 18 investors, at a price per share of $0.83, for an aggregate purchase price of $15.0 million.

In June 2011, we issued and sold 10,135,128 shares of our Series C preferred stock to 17 investors, at a price per share of $0.74, for an aggregate purchase price of $7.5 million.

No underwriters were involved in the foregoing issuances of securities. The securities described in this section (a) of Item 15 were issued to accredited investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The recipients of securities in the transactions described above represented that they were accredited investors and were acquiring the securities for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time and appropriate legends were affixed to the instruments representing such securities issued in such transactions.

(b) Stock option grants

Between January 1, 2011 and March 28, 2014, we issued to certain employees, directors and consultants options to purchase an aggregate of 1,080,479 shares of our common stock, of which, as of March 28, 2014, options to purchase 95,282 shares of our common stock had been exercised or forfeited, and options to purchase 985,197 shares of our common stock remained outstanding at a weighted-average exercise price of $4.79 per share.

The issuances of stock options and the shares of our common stock issuable upon the exercise of the options described in this paragraph (b) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

(c) Issuance of warrant

On December 6, 2011, we issued a warrant to purchase an aggregate of 421,687 shares of Series D preferred stock at a price of $0.83 per share to Lighthouse Capital Partners VI, L.P. On June 2, 2012, this warrant became exercisable for an additional 271,084 shares of Series D preferred stock at a price per share of $0.83, and on October 2, 2012, this warrant became exercisable for an additional 271,085 shares of Series D preferred stock at a price per share of $0.83.

The securities described in this section (c) of Item 15 were issued to Lighthouse Capital Partners VI, L.P. in reliance upon an exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)2) under the Securities Act relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. All certificates representing the issued shares of capital stock described in this Item 15 included appropriate legends setting forth that the securities have not been registered and the applicable restrictions on transfer.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit Number	Description of Exhibit
1.1	Form of Underwriting Agreement
3.1	Certificate of Incorporation of the Registrant, as amended
3.2**	Amended and Restated Bylaws of the Registrant
3.3**	Form of Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering)
3.4**	Form of By-laws of the Registrant (to be effective upon the closing of this offering)
4.1	Specimen Stock Certificate evidencing the shares of common stock
5.1	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
10.1**	2007 Stock Incentive Plan, as amended
10.2**	Form of Incentive Stock Option Agreement under 2007 Stock Incentive Plan
10.3**	Form of Nonstatutory Stock Option Agreement under 2007 Stock Incentive Plan
10.4	2014 Stock Incentive Plan
10.5	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan
10.6	Form of Nonstatutory Stock Option Agreement under 2014 Stock Incentive Plan
10.7†**	License Agreement, dated as of May 22, 2000, as amended, between California Institute of Technology and Insert Therapeutics, Inc.
10.8†**	Exclusive Patent License Agreement, dated as of December 21, 2006, as amended, between the Registrant and Massachusetts Institute of Technology
10.9†**	Patent License Agreement, dated as of August 31, 2007, as amended, between the Registrant and The Research Foundation of State University of New York, on behalf of University of Buffalo
10.10†**	IT-101 Agreement, dated as of June 23, 2009, as amended, between the Registrant and Calando Pharmaceuticals, Inc.
10.11†**	Platform Agreement, dated as of June 23, 2009, as amended, between the Registrant and Calando Pharmaceuticals, Inc.
10.12†**	Letter Agreement, dated as of August 6, 2013, between the Registrant and California Institute of Technology
10.13**	Second Series D Convertible Preferred Stock Purchase Agreement, dated November 30, 2012, as amended

Exhibit Number	Description of Exhibit
10.14**	Commercial Lease Agreement, dated September 8, 2009, between the Registrant and Rivertech Associates II, LLC
10.15**	Loan and Security Agreement, entered into as of December 6, 2011, as amended, between the Registrant and Lighthouse Capital Partners VI, L.P.
10.16**	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors
10.17**	Employment Agreement, dated as of April 8, 2009, by and between Registrant and Oliver Fetzer
10.18**	Warrant to purchase shares of Series B Convertible Preferred Stock issued by the Registrant to Silicon Valley Bank
10.19**	Form of Stock Purchase Warrant of the Registrant to purchase shares of Series C Convertible Preferred Stock
10.20**	Preferred Stock Purchase Warrant to purchase shares of Series D Convertible Preferred Stock issued by the Registrant to Lighthouse Capital Partners VI, L.P., as amended
10.21**	Offer Letter, dated as of January 4, 2012, by and between Registrant and Christopher Guiffre
10.22**	Offer Letter, dated as of April 23, 2011, by and between Registrant and Edward Garmey
10.23**	Stock Option Agreement and Contingent Consideration Award Agreement, dated March 31, 2013, between the Registrant and Oliver Fetzer
10.24**	Stock Option Agreement and Contingent Consideration Award Agreement, dated March 31, 2013, between the Registrant and Alan Crane
10.25**	Change in Control Severance Plan
10.26	2014 Employee Stock Purchase Plan
21.1**	Subsidiaries of the Registrant
23.1	Consent of Deloitte & Touche LLP
23.2	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)
24.1**	Power of Attorney (included on signature page)

** Previously filed.

† Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

(b) Financial Statement Schedules.

Item 17. Undertakings.

(a) The undersigned registrant hereby undertakes to provide to the underwriter, at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

(b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(c) The undersigned hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant has duly caused this Amendment No. 2 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this 31st day of March, 2014.

CERULEAN PHARMA INC.

By: /s/ Oliver S. Fetzer
Oliver S. Fetzer, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 2 to the Registration Statement has been signed by the following persons in the capacities held on the dates indicated.

Signature	Title	Date
/s/ Oliver S. Fetzer Oliver S. Fetzer, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	March 31, 2014
/s/ Christopher D. T. Guiffre Christopher D. T. Guiffre, J.D.	Senior Vice President and Chief Business Officer (principal financial officer)	March 31, 2014
/s/ Karen L. Roberts Karen L. Roberts	Senior Vice President, Finance and Administration (principal accounting officer)	March 31, 2014
* Alan L. Crane	Director	March 31, 2014
* Paul A. Friedman, M.D.	Director	March 31, 2014
* Steven E. Hall, Ph.D.	Director	March 31, 2014
* William T. McKee	Director	March 31, 2014
* William H. Rastetter, Ph.D.	Director	March 31, 2014
* Ram Sasisekharan, Ph.D.	Director	March 31, 2014
* Robert I. Tepper, M.D.	Director	March 31, 2014

*By /s/ Oliver S. Fetzer
Oliver S. Fetzer
Attorney-in-Fact

Exhibit Index

Exhibit Number	Description of Exhibit
1.1	Form of Underwriting Agreement
3.1	Certificate of Incorporation of the Registrant, as amended
3.2**	Amended and Restated Bylaws of the Registrant
3.3**	Form of Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering)
3.4**	Form of By-laws of the Registrant (to be effective upon the closing of this offering)
4.1	Specimen Stock Certificate evidencing the shares of common stock
5.1	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
10.1**	2007 Stock Incentive Plan, as amended
10.2**	Form of Incentive Stock Option Agreement under 2007 Stock Incentive Plan
10.3**	Form of Nonstatutory Stock Option Agreement under 2007 Stock Incentive Plan
10.4	2014 Stock Incentive Plan
10.5	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan
10.6	Form of Nonstatutory Stock Option Agreement under 2014 Stock Incentive Plan
10.7†**	License Agreement, dated as of May 22, 2000, as amended, between California Institute of Technology and Insert Therapeutics, Inc.
10.8†**	Exclusive Patent License Agreement, dated as of December 21, 2006, as amended, between the Registrant and Massachusetts Institute of Technology
10.9†**	Patent License Agreement, dated as of August 31, 2007, as amended, between the Registrant and The Research Foundation of State University of New York, on behalf of University of Buffalo
10.10†**	IT-101 Agreement, dated as of June 23, 2009, as amended, between the Registrant and Calando Pharmaceuticals, Inc.
10.11†**	Platform Agreement, dated as of June 23, 2009, as amended, between the Registrant and Calando Pharmaceuticals, Inc.
10.12†**	Letter Agreement, dated as of August 6, 2013, between the Registrant and California Institute of Technology
10.13**	Second Series D Convertible Preferred Stock Purchase Agreement, dated November 30, 2012, as amended
10.14**	Commercial Lease Agreement, dated September 8, 2009, between the Registrant and Rivertech Associates II, LLC
10.15**	Loan and Security Agreement, entered into as of December 6, 2011, as amended, between the Registrant and Lighthouse Capital Partners VI, L.P.
10.16**	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors
10.17**	Employment Agreement, dated as of April 8, 2009, by and between Registrant and Oliver Fetzer

Exhibit Number	Description of Exhibit
10.18**	Warrant to purchase shares of Series B Convertible Preferred Stock issued by the Registrant to Silicon Valley Bank
10.19**	Form of Stock Purchase Warrant of the Registrant to purchase shares of Series C Convertible Preferred Stock
10.20**	Preferred Stock Purchase Warrant to purchase shares of Series D Convertible Preferred Stock issued by the Registrant to Lighthouse Capital Partners VI, L.P., as amended
10.21**	Offer Letter, dated as of January 4, 2012, by and between Registrant and Christopher Guiffre
10.22**	Offer Letter, dated as of April 23, 2011, by and between Registrant and Edward Garmey
10.23**	Stock Option Agreement and Contingent Consideration Award Agreement, dated March 31, 2013, between the Registrant and Oliver Fetzer
10.24**	Stock Option Agreement and Contingent Consideration Award Agreement, dated March 31, 2013, between the Registrant and Alan Crane
10.25**	Change in Control Severance Plan
10.26	2014 Employee Stock Purchase Plan
21.1**	Subsidiaries of the Registrant
23.1	Consent of Deloitte & Touche LLP
23.2	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)
24.1**	Power of Attorney (included on signature page)

** Previously filed.

† Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

Exhibit 1.1

CERULEAN PHARMA INC.

(a Delaware corporation)

[—] Shares of Common Stock

FORM OF UNDERWRITING AGREEMENT

Dated: [—], 2014

CERULEAN PHARMA INC.

(a Delaware corporation)

[—] Shares of Common Stock

UNDERWRITING AGREEMENT

[—], 2014

Leerink Partners LLC
as Representative of the several Underwriters

c/o Leerink Partners LLC
One Federal Street, Floor 37
Boston, MA 02110

Ladies and Gentlemen:

Cerulean Pharma Inc., a Delaware corporation (the "Company"), confirms its agreement with Leerink Partners LLC ("Leerink") and each of the other Underwriters named in Schedule A hereto (collectively, the "Underwriters," which term shall also include any underwriter substituted as hereinafter provided in Section 10 hereof), for whom Leerink is acting as representative (in such capacity, the "Representative"), with respect to (i) the sale by the Company and the purchase by the Underwriters, acting severally and not jointly, of the respective numbers of shares of common stock, par value $0.0001 per share, of the Company ("Common Stock") set forth in Schedule A hereto and (ii) the grant by the Company to the Underwriters, acting severally and not jointly, of the option described in Section 2(b) hereof to purchase all or any part of [—] additional shares of Common Stock to cover overallotments, if any. The aforesaid [—] shares of Common Stock (the "Initial Securities") to be purchased by the Underwriters and all or any part of the [—] shares of Common Stock subject to the option described in Section 2(b) hereof (the "Option Securities") are herein called, collectively, the "Securities."

The Company understands that the Underwriters propose to make a public offering of the Securities as soon as the Representative deems advisable after this Agreement has been executed and delivered.

The Company has filed with the Securities and Exchange Commission (the "Commission") a registration statement on Form S-1 (No. 333-194442), including the related preliminary prospectus or prospectuses, covering the registration of the sale of the Securities under the Securities Act of 1933, as amended (the "1933 Act"). Promptly after execution and delivery of this Agreement, the Company will prepare and file a prospectus in accordance with the provisions of Rule 430A ("Rule 430A") of the rules and regulations of the Commission under the 1933 Act (the "1933 Act Regulations") and Rule 424(b) ("Rule 424(b)") of the 1933 Act Regulations. The information included in such prospectus that was omitted from such registration statement at the time it became effective but that is deemed to be part of such registration statement at the time it became effective pursuant to Rule 430A(b) is herein called the "Rule 430A Information." Such registration statement, including the amendments thereto, the exhibits thereto and any schedules thereto at the time it became effective, and including the Rule 430A Information, is herein called the "Registration Statement." Any registration statement filed pursuant to Rule 462(b) of the 1933 Act Regulations is herein called the "Rule 462(b) Registration Statement" and, after such filing, the term "Registration Statement" shall include the Rule 462(b) Registration Statement.

Each prospectus used prior to the effectiveness of the Registration Statement, and each prospectus that omitted the Rule 430A Information that was used after such effectiveness and prior to the execution and delivery of this Agreement is herein called a "preliminary prospectus." The final prospectus, in the form first furnished to the Underwriters for use in connection with the offering of the Securities is herein called the "Prospectus." For purposes of this Agreement, all references to the Registration Statement, any preliminary prospectus, the Prospectus or any amendment or supplement to any of the foregoing shall be deemed to include the copy filed with the Commission pursuant to its Electronic Data Gathering, Analysis and Retrieval system or any successor system ("EDGAR").

As used in this Agreement:

"Applicable Time" means [:00 P./A.M.], New York City time, on [—], 2014 or such other time as agreed by the Company and Leerink.

"General Disclosure Package" means any Issuer General Use Free Writing Prospectuses issued at or prior to the Applicable Time, the most recent preliminary prospectus that is distributed to investors prior to the Applicable Time and the information included on Schedule B-1 hereto, all considered together.

"Issuer Free Writing Prospectus" means any "issuer free writing prospectus," as defined in Rule 433 of the 1933 Act Regulations ("Rule 433"), including without limitation any "free writing prospectus" (as defined in Rule 405 of the 1933 Act Regulations ("Rule 405")) relating to the Securities that is (i) required to be filed with the Commission by the Company, (ii) a "road show that is a written communication" within the meaning of Rule 433(d)(8)(i), whether or not required to be filed with the Commission, or (iii) exempt from filing with the Commission pursuant to Rule 433(d)(5)(i) because it contains a description of the Securities or of the offering that does not reflect the final terms, in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company's records pursuant to Rule 433(g).

"Issuer General Use Free Writing Prospectus" means any Issuer Free Writing Prospectus that is intended for general distribution to prospective investors (other than a "*bona fide* electronic road show," as defined in Rule 433 (the "Bona Fide Electronic Road Show")), as evidenced by its being specified in Schedule B-2 hereto.

"Issuer Limited Use Free Writing Prospectus" means any Issuer Free Writing Prospectus that is not an Issuer General Use Free Writing Prospectus.

"Testing-the-Waters Communication" means any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the 1933 Act.

"Written Testing-the-Waters Communication" means any Testing-the-Waters Communication that is a written communication within the meaning of Rule 405 under the 1933 Act.

SECTION 1. Representations and Warranties.

(a) *Representations and Warranties by the Company*. The Company represents and warrants to each Underwriter as of the date hereof, the Applicable Time, the Closing Time (as defined below) and any Date of Delivery (as defined below), and agrees with each Underwriter, as follows:

(i) Registration Statement and Prospectuses. Each of the Registration Statement and any amendment thereto has become effective under the 1933 Act. No stop order suspending the effectiveness of the Registration Statement or any post-effective amendment thereto has been issued under the 1933 Act, no order preventing or suspending the use of any preliminary prospectus or the Prospectus has been issued and no proceedings for any of those purposes have been instituted or are pending or, to the Company's knowledge, contemplated. The Company has complied with each request (if any) from the Commission for additional information.

Each of the Registration Statement and any post-effective amendment thereto, at the time it became effective, complied in all material respects with the requirements of the 1933 Act and the 1933 Act Regulations. Each preliminary prospectus, the Prospectus and any amendment or supplement thereto, at the time each was filed with the Commission, complied in all material respects with the requirements of the 1933 Act and the 1933 Act Regulations. Each preliminary prospectus delivered to the Underwriters for use in connection with this offering and the Prospectus was or will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(ii) Accurate Disclosure. Neither the Registration Statement nor any amendment thereto, at its effective time, at the Closing Time or at any Date of Delivery, contained, contains or will contain an untrue statement of a material fact or omitted, omits or will omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading. As of the Applicable Time, none of (A) the General Disclosure Package, (B) any individual Issuer Limited Use Free Writing Prospectus, when considered together with the General Disclosure Package, nor (C) any individual Written Testing-the-Waters Communication, when considered together with the General Disclosure Package, included, includes or will include an untrue statement of a material fact or omitted, omits or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. Neither the Prospectus nor any amendment or supplement thereto (including any prospectus wrapper), as of its issue date, at the time of any filing with the Commission pursuant to Rule 424(b), at the Closing Time or at any Date of Delivery, included, includes or will include an untrue statement of a material fact or omitted, omits or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading.

The representations and warranties in this subsection shall not apply to statements in or omissions from the Registration Statement (or any amendment thereto), the General Disclosure Package or the Prospectus (or any amendment or supplement thereto, including any prospectus wrapper) made in reliance upon and in conformity with written information furnished to the Company by any Underwriter through Leerink expressly for use therein. For purposes of this Agreement, the only information so furnished shall be the information in the [first paragraph under the heading "Underwriting—Commissions and Discounts," the information in the second, third and fourth paragraphs under the heading "Underwriting—Price Stabilization, Short Positions and Penalty Bids" and the information under the heading "Underwriting—Electronic Distribution"] in each case contained in the Prospectus (collectively, the "Underwriter Information").

(iii) Issuer Free Writing Prospectuses. No Issuer Free Writing Prospectus conflicts or will conflict with the information contained in the Registration Statement or the Prospectus, and any preliminary or other prospectus deemed to be a part thereof that has not been superseded or modified. The Company has made available a Bona Fide Electronic Road Show in compliance with Rule 433(d)(8)(ii) such that no filing of any "road show" (as defined in Rule 433(h)) is required in connection with the offering of the Securities.

(iv) Testing-the-Waters Materials. The Company (A) has not engaged in any Testing-the-Waters Communication other than Testing-the-Waters Communications with the consent of the Representative with entities that are qualified institutional buyers within the meaning of Rule 144A under the 1933 Act or institutions that are accredited investors within the meaning of Rule 501 under the 1933 Act and (B) has not authorized anyone other than the Representative to engage in Testing-the-Waters Communications. The Company reconfirms that the Representative has been authorized to act on its behalf in undertaking Testing-the-Waters Communications. The Company has not distributed any Written Testing-the-Waters Communications other than those listed on Schedule B-3 hereto.

(v) Company Not Ineligible Issuer. At the time of filing the Registration Statement and any post-effective amendment thereto, at the earliest time thereafter that the Company or another offering participant made a *bona fide* offer (within the meaning of Rule 164(h)(2) of the 1933 Act Regulations) of the Securities and at the date hereof, the Company was not and is not an "ineligible issuer," as defined in Rule 405, without taking account of any determination by the Commission pursuant to Rule 405 that it is not necessary that the Company be considered an ineligible issuer.

(vi) Emerging Growth Company Status. From the time of the initial confidential submission of the Registration Statement to the Commission (or, if earlier, the first date on which the Company engaged directly or through any Person authorized to act on its behalf in any Testing-the-Waters Communication) through the date hereof, the Company has been and is an "emerging growth company," as defined in Section 2(a) of the 1933 Act (an "Emerging Growth Company").

(vii) Independent Accountants. The accountants who certified the financial statements and supporting schedules included in the Registration Statement, the General Disclosure Package and the Prospectus are independent public accountants as required by the 1933 Act, the 1933 Act Regulations and the Public Company Accounting Oversight Board.

(viii) Financial Statements; Non-GAAP Financial Measures. The financial statements included in the Registration Statement, the General Disclosure Package and the Prospectus, together with the related schedules and notes, present fairly, in all material respects, the financial position of the Company and its consolidated subsidiary at the dates indicated and the statement of operations, stockholders' equity and cash flows of the Company and its consolidated subsidiary for the periods specified; said financial statements have been prepared in conformity with U.S. generally accepted accounting principles ("GAAP") applied on a consistent basis throughout the periods involved, except in the case of unaudited, interim financial statements, subject to normal year-end audit adjustments and the exclusion of certain footnotes as permitted by the applicable rules of the Commission. The supporting schedules, if any, present fairly, in all material respects, in accordance with GAAP the information required to be stated therein. The selected financial data and the summary financial information included in the Registration Statement, the General Disclosure Package and the Prospectus present fairly, in all material respects, the information shown therein and have been compiled on a basis consistent with that of the audited financial statements included therein. The pro forma financial statements and the related notes thereto included in the Registration Statement, the General Disclosure Package and the Prospectus present fairly the information shown therein, have been prepared in accordance with the Commission's rules and guidelines with respect to pro forma financial statements and have been properly complied on the bases described therein, and the assumptions used in the preparation thereof are reasonable and the adjustments used therein are appropriate to give effect to the transactions and circumstances referred to therein.[1] Except as included therein, no historical or pro forma financial statements or supporting schedules are required to be included or incorporated by reference in the Registration Statement, the General Disclosure Package or the Prospectus under the 1933 Act or the 1933 Act Regulations.

(ix) No Material Adverse Change in Business. Except as otherwise stated therein, since the respective dates as of which information is given in the Registration Statement, the General Disclosure Package or the Prospectus, (A) there has been no material adverse change in the condition, financial or otherwise, or in the earnings, business affairs or business prospects of the Company and its subsidiary considered as one enterprise, whether or not arising in the ordinary course of business (a "Material Adverse Effect"), (B) there have been no transactions entered into by the Company or its subsidiary, other than those in the ordinary course of business, which are material with respect to the Company and its subsidiary considered as one enterprise, and (C) there has been no dividend or distribution of any kind declared, paid or made by the Company on any class of its capital stock.

(x) Good Standing of the Company. The Company has been duly organized and is validly existing as a corporation in good standing under the laws of the State of Delaware and has corporate power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement, the General Disclosure Package and the Prospectus and to enter into and perform its obligations under this Agreement; and the Company is duly qualified as a foreign corporation to transact business and is in good standing in each jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except where the failure so to qualify or to be in good standing would not result in a Material Adverse Effect.

(xi) Good Standing of Subsidiary. The subsidiary of the Company (the "Subsidiary") has been duly organized and is validly existing in good standing under the laws of the jurisdiction of its incorporation or organization, has corporate or similar power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement, the General Disclosure Package and the Prospectus and is duly qualified to transact business and is in good standing in each jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except where the failure to so qualify or to be in good standing would not result in a Material Adverse Effect. Except as otherwise disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, all of the issued and outstanding capital stock of the Subsidiary has been duly authorized and validly issued, is fully paid and non-assessable and is owned by the Company, directly or through subsidiaries, free and clear of any security interest, mortgage, pledge, lien, encumbrance, claim or equity. None of the outstanding shares of capital stock of the Subsidiary were issued in violation of the preemptive or similar rights of any securityholder of such Subsidiary. The only subsidiary of the Company is the subsidiary listed on Exhibit 21 to the Registration Statement.

(xii) Capitalization. The authorized, issued and outstanding shares of capital stock of the Company are as set forth in the Registration Statement, the General Disclosure Package and the Prospectus in the column entitled "Actual" under the caption "Capitalization" (except for

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[1] Note to Wilmer: The company is providing pro forma financial information giving effect to the offering, so we think this language is appropriate.

subsequent issuances, if any, pursuant to this Agreement, pursuant to reservations, agreements or employee benefit plans referred to in the Registration Statement, the General Disclosure Package and the Prospectus or pursuant to the exercise of convertible securities or options referred to in the Registration Statement, the General Disclosure Package and the Prospectus). The outstanding shares of capital stock of the Company have been duly authorized and validly issued and are fully paid and non-assessable. None of the outstanding shares of capital stock of the Company were issued in violation of the preemptive or other similar rights of any securityholder of the Company.

(xiii) Authorization of Agreement. This Agreement has been duly authorized, executed and delivered by the Company.

(xiv) Authorization and Description of Securities. The Securities to be purchased by the Underwriters from the Company have been duly authorized for issuance and sale to the Underwriters pursuant to this Agreement and, when issued and delivered by the Company pursuant to this Agreement against payment of the consideration set forth herein, will be validly issued and fully paid and non-assessable; and the issuance of the Securities is not subject to the preemptive or other similar rights of any securityholder of the Company, except as have been duly and validly waived in writing as of the date of this Agreement, copies of such waivers having been made available to you. The Common Stock conforms, in all material respects, to all statements relating thereto contained in the Registration Statement, the General Disclosure Package and the Prospectus and such description conforms, in all material respects, to the rights set forth in the instruments defining the same. No holder of Securities will be subject to personal liability by reason of being such a holder.

(xv) Registration Rights. There are no persons with registration rights or other similar rights to have any securities registered for sale pursuant to the Registration Statement or otherwise registered for sale or sold by the Company under the 1933 Act pursuant to this Agreement, other than those rights that have been disclosed in the Registration Statement, the General Disclosure Package and the Prospectus and have been waived.

(xvi) Absence of Violations, Defaults and Conflicts. Neither the Company nor its subsidiary is (A) in violation of its charter, by-laws or similar organizational document, (B) in default in the performance or observance of any obligation, agreement, covenant or condition contained in any contract, indenture, mortgage, deed of trust, loan or credit agreement, note, lease or other agreement or instrument to which the Company or its subsidiary is a party or by which either of them may be bound or to which any of the properties or assets of the Company or its subsidiary is subject (collectively, "Agreements and Instruments"), except for such defaults that would not, singly or in the aggregate, result in a Material Adverse Effect, or (C) in violation of any law, statute, rule, regulation, judgment, order, writ or decree of any arbitrator, court, governmental body, regulatory body, administrative agency or other authority, body or agency having jurisdiction over the Company or its subsidiary or any of their respective properties, assets or operations (each, a "Governmental Entity"), except for such violations that would not, singly or in the aggregate, result in a Material Adverse Effect. The execution, delivery and performance of this Agreement and the consummation of the transactions contemplated herein and in the Registration Statement, the General Disclosure Package and the Prospectus (including the issuance and sale of the Securities and the use of the proceeds from the sale of the Securities as described therein under the caption "Use of Proceeds") and compliance by the Company with its obligations hereunder have been duly authorized by all necessary corporate action and do not and will not, whether with or without the giving of notice or passage of time or both, conflict with or constitute a breach of, or default or Repayment Event (as defined below) under, or result in the creation or imposition of any lien, charge or encumbrance upon any properties or assets of the

Company or its subsidiary pursuant to, the Agreements and Instruments (except for such conflicts, breaches, defaults or Repayment Events or liens, charges or encumbrances that would not, singly or in the aggregate, result in a Material Adverse Effect), nor will such action result in any violation of the provisions of the charter, by-laws or similar organizational document of the Company or its subsidiary or any law, statute, rule, regulation, judgment, order, writ or decree of any Governmental Entity. As used herein, a "Repayment Event" means any event or condition which gives the holder of any note, debenture or other evidence of indebtedness (or any person acting on such holder's behalf) the right to require the repurchase, redemption or repayment of all or a portion of such indebtedness by the Company or its subsidiary.

(xvii) Absence of Labor Dispute. No labor dispute with the employees of the Company or its subsidiary exists or, to the knowledge of the Company, is imminent, and the Company is not aware of any existing or imminent labor disturbance by the employees of any of its or its subsidiary's principal suppliers, manufacturers, customers or contractors, which, in either case, would result in a Material Adverse Effect.

(xviii) Absence of Proceedings. Except as disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, there is no action, suit, proceeding, inquiry or investigation before or brought by any Governmental Entity now pending or, to the knowledge of the Company, threatened, against or affecting the Company or its subsidiary, which would reasonably be expected to result in a Material Adverse Effect, or which would reasonably be expected to materially and adversely affect their respective properties or assets or the consummation of the transactions contemplated in this Agreement or the performance by the Company of its obligations hereunder; and the aggregate of all pending legal or governmental proceedings to which the Company or its subsidiary is a party or of which either of their respective properties or assets is the subject which are not described in the Registration Statement, the General Disclosure Package and the Prospectus, including ordinary routine litigation incidental to the business, would not reasonably be expected to result in a Material Adverse Effect.

(xix) Accuracy of Exhibits. There are no contracts or documents which are required to be described in the Registration Statement, the General Disclosure Package or the Prospectus or to be filed as exhibits to the Registration Statement which have not been so described and filed as required.

(xx) Absence of Further Requirements. No filing with, or authorization, approval, consent, license, order, registration, qualification or decree of, any Governmental Entity is necessary or required for the performance by the Company of its obligations hereunder, in connection with the offering, issuance or sale of the Securities hereunder or the consummation of the transactions contemplated by this Agreement, except such as have been already obtained or as may be required under the 1933 Act, the 1933 Act Regulations, the rules of the NASDAQ Stock Market LLC, state securities laws or the rules of the Financial Industry Regulatory Authority, Inc. ("FINRA").

(xxi) Possession of Licenses and Permits. The Company and its subsidiary possess such permits, licenses, approvals, consents and other authorizations (collectively, "Governmental Licenses") issued by the appropriate Governmental Entities necessary to conduct the business now operated by them, except where the failure so to possess would not, singly or in the aggregate, result in a Material Adverse Effect. The Company and its subsidiary are in compliance with the terms and conditions of all Governmental Licenses, except where the failure so to comply would not, singly or in the aggregate, result in a Material Adverse Effect. All of the

Governmental Licenses are valid and in full force and effect, except where the invalidity of such Governmental Licenses or the failure of such Governmental Licenses to be in full force and effect would not, singly or in the aggregate, result in a Material Adverse Effect. Neither the Company nor its subsidiary has received any notice of proceedings relating to the revocation or modification of any Governmental Licenses which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, would result in a Material Adverse Effect.

(xxii) Title to Property. The Company and its subsidiary have good and marketable title to all real property owned by them and good title to all other properties owned by them (excluding for the purpose of this Section (1)(a)(xxii), Intellectual Property (as defined below)), in each case, free and clear of all mortgages, pledges, liens, security interests, claims, restrictions or encumbrances of any kind except such as (A) are described in the Registration Statement, the General Disclosure Package and the Prospectus or (B) do not, singly or in the aggregate, materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company or its subsidiary; and all of the leases and subleases material to the business of the Company and its subsidiary, considered as one enterprise, and under which the Company or its subsidiary holds properties described in the Registration Statement, the General Disclosure Package or the Prospectus, are in full force and effect, and neither the Company nor its subsidiary has any notice of any material claim of any sort that has been asserted by anyone adverse to the rights of the Company or its subsidiary under any of the leases or subleases mentioned above, or affecting or questioning the rights of the Company or such subsidiary to the continued possession of the leased or subleased premises under any such lease or sublease.

(xxiii) Intellectual Property. To the knowledge of the Company, the Company owns or has valid, binding and enforceable licenses or other rights under the patents, patent applications, licenses, inventions, copyrights, know how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures), trademarks, service marks, trade names or other intellectual property reasonably necessary to carry on the business of the Company as described in the Registration Statement, the General Disclosure Package and the Prospectus (collectively, the "Intellectual Property"); the patents, trademarks, and copyrights, if any, included within the Intellectual Property are valid, enforceable, and subsisting; other than as disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, (A) the Company is not obligated to pay a material royalty, grant a license to, or provide other material consideration to any third party in connection with the Intellectual Property, (B) the Company has not received any notice of any claim of infringement, misappropriation or conflict with any asserted rights of others with respect to any of the Company's drug candidates, processes or Intellectual Property, (C) to the knowledge of the Company, neither the sale nor use of any of the discoveries, inventions, drug candidates or processes of the Company referred to in the Registration Statement, the General Disclosure Package or the Prospectus do or will, to the knowledge of the Company, infringe, misappropriate or violate any right or valid patent claim of any third party, and (D) to the knowledge of the Company, no third party has any ownership right in or to any Intellectual Property that is owned by the Company, other than any co-owner of any patent constituting Intellectual Property who is listed on the records of the U.S. Patent and Trademark Office (the "USPTO") and any co-owner of any patent application constituting Intellectual Property who is named in such patent application, and, to the knowledge of the Company, no third party has any ownership right in or to any Intellectual Property in any field of use that is exclusively licensed to the Company, other than any licensor to the Company of such Intellectual Property.

(xxiv) Patents and Patent Applications. All patents and patent applications owned by or licensed to the Company or under which the Company has rights have, to the knowledge of the Company, been duly and properly filed and maintained; to the knowledge of the Company, the parties prosecuting such applications have complied with their duty of candor and disclosure to the USPTO in connection with such applications; and the Company is not aware of any facts required to be disclosed to the USPTO that were not disclosed to the USPTO and which would preclude the grant of a patent in connection with any such application or would reasonably be expected to form the basis of a finding of invalidity with respect to any patents that have issued with respect to such applications.

(xxv) Environmental Laws. Except as described in the Registration Statement, the General Disclosure Package and the Prospectus or would not, singly or in the aggregate, result in a Material Adverse Effect, (A) neither the Company nor its subsidiary is in violation of any federal, state, local or foreign statute, law, rule, regulation, ordinance, code, policy or rule of common law or any judicial or administrative interpretation thereof, including any judicial or administrative order, consent, decree or judgment, relating to pollution or protection of human health, the environment (including, without limitation, ambient air, surface water, groundwater, land surface or subsurface strata) or wildlife, including, without limitation, laws and regulations relating to the release or threatened release of chemicals, pollutants, contaminants, wastes, toxic substances, hazardous substances, petroleum or petroleum products, asbestos-containing materials or mold (collectively, "Hazardous Materials") or to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or handling of Hazardous Materials (collectively, "Environmental Laws"), (B) the Company and its subsidiary have all permits, authorizations and approvals required under any applicable Environmental Laws and are each in compliance with their requirements, (C) there are no pending or, to the knowledge of the Company threatened, administrative, regulatory or judicial actions, suits, demands, demand letters, claims, liens, notices of noncompliance or violation, investigation or proceedings relating to any Environmental Law against the Company or its subsidiary and (D) there are no events or circumstances that would reasonably be expected to form the basis of an order for clean-up or remediation, or an action, suit or proceeding by any private party or Governmental Entity, against or affecting the Company or its subsidiary relating to Hazardous Materials or any Environmental Laws.

(xxvi) Accounting Controls and Disclosure Controls. The Company and its subsidiary have established effective internal control over financial reporting (as defined under Rule 13-a15 and 15d-15 under the rules and regulations of the Commission under the 1934 Act (the "1934 Act Regulations")) and a system of internal accounting controls sufficient to provide reasonable assurances that (A) transactions are executed in accordance with management's general or specific authorization; (B) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain accountability for assets; (C) access to assets is permitted only in accordance with management's general or specific authorization; and (D) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. Except as described in the Registration Statement, the General Disclosure Package and the Prospectus, since the end of the Company's most recent audited fiscal year, there has been (1) no material weakness in the Company's internal control over financial reporting (whether or not remediated) and (2) no change in the Company's internal control over financial reporting that has materially adversely affected, or is reasonably likely to materially adversely affect, the Company's internal control over financial reporting.

(xxvii) Tests and Preclinical and Clinical Trials. The studies, tests and preclinical and clinical trials conducted by the Company (“Company Trials”), and, to the Company’s knowledge, the investigator-sponsored trials (“ISTs”), that are described in the Registration Statement, the General Disclosure Package and the Prospectus were and, if still pending, are being conducted in all material respects in accordance with the protocols submitted to the U.S. Food and Drug Administration (the “FDA”) or any foreign governmental body exercising comparable authority, procedures and controls pursuant to, where applicable, accepted professional and scientific standards, and all applicable laws and regulations. The descriptions of the Company Trials and, to the Company’s knowledge, the ISTs, and the results thereof, contained in the Registration Statement, the General Disclosure Package and the Prospectus are accurate and complete in all material respects. The Company is not aware of any other studies, tests or preclinical and clinical trials other than the Company Trials and the ISTs, the results of which call into question the results described in the Registration Statement, the General Disclosure Package and the Prospectus. The Company has not received any notices or correspondence from the FDA, any foreign, state or local governmental body exercising comparable authority or any Institutional Review Board requiring the termination, suspension, material modification or clinical hold of the Company Trials or the ISTs, other than ordinary course communications with respect to modifications in connection with the design and implementation of such trials, copies of which communications have been made available to you.

(xxviii) Payment of Taxes. All United States federal income tax returns of the Company and its subsidiary required by law to be filed have been filed and all taxes shown by such returns or otherwise assessed, which are due and payable, have been paid, except assessments against which appeals have been or will be promptly taken and as to which adequate reserves have been provided. The United States federal income tax returns of the Company through the fiscal year ended December 31, [2012] have been settled and no assessment in connection therewith has been made against the Company. The Company and its subsidiary have filed all other tax returns that are required to have been filed by them pursuant to applicable foreign, state, local or other law except insofar as the failure to file such returns would not result in a Material Adverse Effect, and have paid all taxes due pursuant to such returns or pursuant to any assessment received by the Company and its subsidiary, except for such taxes, if any, as are being contested in good faith and as to which adequate reserves have been established by the Company. The charges, accruals and reserves on the books of the Company in respect of any income and corporation tax liability for any years not finally determined are adequate to meet any assessments or re-assessments for additional income tax for any years not finally determined, except to the extent of any inadequacy that would not result in a Material Adverse Effect.

(xxix) Insurance. The Company and its subsidiary carry or are entitled to the benefits of insurance, with financially sound and reputable insurers, in such amounts and covering such risks as is generally maintained by companies of established repute engaged in the same or similar business, and all such insurance is in full force and effect. The Company has no reason to believe that it or its subsidiary will not be able (A) to renew its existing insurance coverage as and when such policies expire or (B) to obtain comparable coverage from similar institutions as may be necessary or appropriate to conduct its business as now conducted and at a cost that would not result in a Material Adverse Effect. Neither of the Company nor its subsidiary has been denied any insurance coverage which it has sought or for which it has applied.

(xxx) Investment Company Act. The Company is not required, and upon the issuance and sale of the Securities as herein contemplated and the application of the net proceeds therefrom as described in the Registration Statement, the General Disclosure Package and the Prospectus will not be required, to register as an “investment company” under the Investment Company Act of 1940, as amended (the “1940 Act”).

(xxxi) Absence of Manipulation. Neither the Company nor, to the Company's knowledge, any affiliate of the Company has taken, nor will the Company or any affiliate take, directly or indirectly any action which is designed, or would reasonably be expected, to cause or result in, or which constitutes, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Securities or to result in a violation of Regulation M under the 1934 Act.

(xxxii) Foreign Corrupt Practices Act. None of the Company, its subsidiary or, to the knowledge of the Company, any director, officer, agent, employee, affiliate or other person acting on behalf of the Company or its subsidiary is aware of or has taken any action, directly or indirectly, that would result in a violation by such persons of the Foreign Corrupt Practices Act of 1977, as amended, and the rules and regulations thereunder (the "FCPA"), including, without limitation, making use of the mails or any means or instrumentality of interstate commerce corruptly in furtherance of an offer, payment, promise to pay or authorization of the payment of any money, or other property, gift, promise to give, or authorization of the giving of anything of value to any "foreign official" (as such term is defined in the FCPA) or any foreign political party or official thereof or any candidate for foreign political office, in contravention of the FCPA and the Company and, to the knowledge of the Company, its affiliates have conducted their businesses in compliance with the FCPA and have instituted and maintain policies and procedures designed to ensure, and which are reasonably expected to continue to ensure, continued compliance therewith.

(xxxiii) Money Laundering Laws. The operations of the Company and its subsidiary are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all jurisdictions, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any Governmental Entity (collectively, the "Money Laundering Laws"); and no action, suit or proceeding by or before any Governmental Entity involving the Company or its subsidiary with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(xxxiv) OFAC. None of the Company, its subsidiary or, to the knowledge of the Company, any director, officer, agent, employee, affiliate or representative of the Company or its subsidiary is an individual or entity ("Person") currently the subject or target of any sanctions administered or enforced by the United States Government, including, without limitation, the U.S. Department of the Treasury's Office of Foreign Assets Control, the United Nations Security Council, the European Union, Her Majesty's Treasury, or other relevant sanctions authority (collectively, "Sanctions"), nor is the Company located, organized or resident in a country or territory that is the subject of Sanctions; and the Company will not directly or indirectly use the proceeds of the sale of the Securities, or lend, contribute or otherwise make available such proceeds to any subsidiaries, joint venture partners or other Person, to fund any activities of or business with any Person, or in any country or territory, that, at the time of such funding, is the subject of Sanctions or in any other manner that will result in a violation by any Person (including any Person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions.

(xxxv) [INTENTIONALLY OMITTED]

(xxxvi) Lending Relationship. Except as disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, the Company (i) does not have any material lending or other relationship with any banking or lending affiliate of any Underwriter and (ii) does not intend to use any of the proceeds from the sale of the Securities to repay any outstanding debt owed to any affiliate of any Underwriter.

(xxxvii) Statistical and Market-Related Data. Any statistical and market-related data included in the Registration Statement, the General Disclosure Package or the Prospectus are based on or derived from sources that the Company believes, after reasonable inquiry, to be reliable and accurate and, to the extent required, the Company has obtained the written consent to the use of such data from such sources.

(xxxviii) Rating of Debt Securities. The Company has no debt securities or preferred stock that is rated by any "nationally recognized statistical rating organization" (as that term is defined by the Commission for purposes of Rule 436(g)(2) under the 1933 Act).

(b) *Officer's Certificates*. Any certificate signed by any officer of the Company or its subsidiary delivered to the Representative or to counsel for the Underwriters shall be deemed a representation and warranty by the Company to each Underwriter as to the matters covered thereby.

SECTION 2. Sale and Delivery to Underwriters; Closing.

(a) *Initial Securities*. On the basis of the representations and warranties herein contained and subject to the terms and conditions herein set forth, the Company agrees to sell to each Underwriter, severally and not jointly, and each Underwriter, severally and not jointly, agrees to purchase from the Company, at the price per share set forth in Schedule A, that number of Initial Securities set forth in Schedule A opposite the name of such Underwriter, plus any additional number of Initial Securities which such Underwriter may become obligated to purchase pursuant to the provisions of Section 10 hereof, subject, in each case, to such adjustments among the Underwriters as Leerink in its sole discretion shall make to eliminate any sales or purchases of fractional shares.

(b) *Option Securities*. In addition, on the basis of the representations and warranties herein contained and subject to the terms and conditions herein set forth, the Company hereby grants an option to the Underwriters, severally and not jointly, to purchase up to an additional [—] shares of Common Stock, at the price per share set forth in Schedule A, less an amount per share equal to any dividends or distributions declared by the Company and payable on the Initial Securities but not payable on the Option Securities. The option hereby granted may be exercised for 30 days after the date hereof and may be exercised in whole or in part at any time from time to time only for the purpose of covering overallotments made in connection with the offering and distribution of the Initial Securities upon notice by the Representative to the Company setting forth the number of Option Securities as to which the several Underwriters are then exercising the option and the time and date of payment and delivery for such Option Securities. Any such time and date of delivery (a "Date of Delivery") shall be determined by the Representative, but any Date of Delivery occurring after the Closing Time shall not be later than seven full business days nor earlier than two full business days after the exercise of said option, nor in any event prior to the Closing Time. If the option is exercised as to all or any portion of the Option Securities, each of the Underwriters, acting severally and not jointly, will purchase that proportion of the total number of Option Securities then being purchased which the number of Initial Securities set forth in Schedule A opposite the name of such Underwriter bears to the total number of Initial Securities, subject, in each case, to such adjustments as Leerink in its sole discretion shall make to eliminate any sales or purchases of fractional shares.

(c) *Payment*. Payment of the purchase price for, and delivery of certificates for, the Initial Securities shall be made at the offices of Ropes & Gray LLP, Prudential Tower, 800 Boylston Street, Boston, MA 02199, or at such other place as shall be agreed upon by the Representative and the Company, at 9:00 A.M. (New York City time) on the third (fourth, if the pricing occurs after 4:30 P.M. (New York City time) on any given day) business day after the date hereof (unless postponed in accordance with the provisions of Section 10), or such other time not later than ten business days after such date as shall be agreed upon by the Representative and the Company (such time and date of payment and delivery being herein called "Closing Time"). Delivery of the Initial Securities at the Closing Time shall be made through the facilities of The Depository Trust Company unless the Representative shall otherwise instruct.

In addition, in the event that any or all of the Option Securities are purchased by the Underwriters, payment of the purchase price for, and delivery of certificates for, such Option Securities shall be made at the above-mentioned offices, or at such other place as shall be agreed upon by the Representative and the Company, on each Date of Delivery as specified in the notice from Leerink to the Company. Delivery of the Option Securities on each such Date of Delivery shall be made through the facilities of The Depository Trust Company unless the Representative shall otherwise instruct.

Payment shall be made to the Company by wire transfer of immediately available funds to a bank account designated by the Company against delivery to the Representative for the respective accounts of the Underwriters of certificates for the Securities to be purchased by them. It is understood that each Underwriter has authorized the Representative, for its account, to accept delivery of, receipt for, and make payment of the purchase price for, the Initial Securities and the Option Securities, if any, which it has agreed to purchase. Leerink, individually and not as representative of the Underwriters, may (but shall not be obligated to) make payment of the purchase price for the Initial Securities or the Option Securities, if any, to be purchased by any Underwriter whose funds have not been received by the Closing Time or the relevant Date of Delivery, as the case may be, but such payment shall not relieve such Underwriter from its obligations hereunder.

SECTION 3. Covenants of the Company. The Company covenants with each Underwriter as follows:

(a) *Compliance with Securities Regulations and Commission Requests*. The Company, subject to Section 3(b), will comply with the requirements of Rule 430A, and will notify the Representative promptly, and confirm the notice in writing, (i) when any post-effective amendment to the Registration Statement shall become effective or any amendment or supplement to the Prospectus shall have been filed, (ii) of the receipt of any comments from the Commission, (iii) of any request by the Commission for any amendment to the Registration Statement or any amendment or supplement to the Prospectus or for additional information, (iv) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or any post-effective amendment or of any order preventing or suspending the use of any preliminary prospectus or the Prospectus, or of the suspension of the qualification of the Securities for offering or sale in any jurisdiction, or of the initiation or threatening of any proceedings for any of such purposes or of any examination pursuant to Section 8(d) or 8(e) of the 1933 Act concerning the Registration Statement and (v) if the Company becomes the subject of a proceeding under Section 8A of the 1933 Act in connection with the offering of the Securities. The Company will effect all filings required under Rule 424(b), in the manner and within the time period required by Rule 424(b) (without reliance on Rule 424(b)(8)), and will take such steps as it deems necessary to ascertain promptly whether the form of prospectus transmitted for filing under Rule 424(b) was received for filing by the Commission and, in the event that it was not, it will promptly file such prospectus. The Company will make every reasonable effort to prevent the issuance of any stop order, prevention or suspension and, if any such order is issued, to obtain the lifting thereof at the earliest possible moment.

(b) *Continued Compliance with Securities Laws*. The Company will comply with the 1933 Act and the 1933 Act Regulations so as to permit the completion of the distribution of the Securities as contemplated in this Agreement and in the Registration Statement, the General Disclosure Package and the Prospectus. If at any time when a prospectus relating to the Securities is (or, but for the exception afforded by Rule 172 of the 1933 Act Regulations ("Rule 172"), would be) required by the 1933 Act to be delivered in connection with sales of the Securities, any event shall occur or condition shall exist as a result of which it is necessary, in the opinion of counsel for the Underwriters or for the Company, to (i) amend the Registration Statement in order that the Registration Statement will not include an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading, (ii) amend or supplement the General Disclosure Package or the Prospectus in order that the General Disclosure Package or the Prospectus, as the case may be, will not include any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein not misleading in the light of the circumstances existing at the time it is delivered to a purchaser or (iii) amend the Registration Statement or amend or supplement the General Disclosure Package or the Prospectus, as the case may be, in order to comply with the requirements of the 1933 Act or the 1933 Act Regulations, the Company will promptly (A) give the Representative notice of such event, (B) prepare any amendment or supplement as may be necessary to correct such statement or omission or to make the Registration Statement, the General Disclosure Package or the Prospectus comply with such requirements and, a reasonable amount of time prior to any proposed filing or use, furnish the Representative with copies of any such amendment or supplement and (C) file with the Commission any such amendment or supplement; provided that the Company shall not file or use any such amendment or supplement to which the Representative or counsel for the Underwriters shall reasonably object. The Company will furnish to the Underwriters such number of copies of such amendment or supplement as the Underwriters may reasonably request. The Company has given the Representative notice of any filings made pursuant to the 1934 Act or the 1934 Act Regulations within 48 hours prior to the Applicable Time; the Company will give the Representative notice of its intention to make any such filing from the Applicable Time to the Closing Time and will furnish the Representative with copies of any such documents a reasonable amount of time prior to such proposed filing, as the case may be, and will not file or use any such document to which the Representative or counsel for the Underwriters shall reasonably object.

(c) *Delivery of Registration Statements*. The Company has furnished or will deliver to the Representative and counsel for the Underwriters, without charge, signed copies of the Registration Statement as originally filed and each amendment thereto (including exhibits filed therewith) and signed copies of all consents and certificates of experts, and will also deliver to the Representative, without charge, a conformed copy of the Registration Statement as originally filed and each amendment thereto (without exhibits) for each of the Underwriters. The copies of the Registration Statement and each amendment thereto furnished to the Underwriters will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(d) *Delivery of Prospectuses*. The Company has delivered to each Underwriter, without charge, as many copies of each preliminary prospectus as such Underwriter reasonably requested, and the Company hereby consents to the use of such copies for purposes permitted by the 1933 Act. The Company will furnish to each Underwriter, without charge, during the period when a prospectus relating to the Securities is (or, but for the exception afforded by Rule 172, would be) required to be delivered under the 1933 Act, such number of copies of the Prospectus (as amended or supplemented) as such Underwriter may reasonably request. The Prospectus and any amendments or supplements thereto furnished to the Underwriters will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(e) *Blue Sky Qualifications*. The Company will use its best efforts, in cooperation with the Underwriters, to qualify the Securities for offering and sale under the applicable securities laws of such states and other jurisdictions (domestic or foreign) as the Representative may reasonably designate and to maintain such qualifications in effect so long as required to complete the distribution of the Securities; provided, however, that the Company shall not be obligated to file any general consent to service of process or to qualify as a foreign corporation or as a dealer in securities in any jurisdiction in which it is not so qualified or to subject itself to taxation in respect of doing business in any jurisdiction in which it is not otherwise so subject.

(f) *Rule 158*. The Company will timely file such reports pursuant to the 1934 Act as are necessary in order to make generally available to its securityholders as soon as practicable an earnings statement for the purposes of, and to provide to the Underwriters the benefits contemplated by, the last paragraph of Section 11(a) of the 1933 Act.

(g) *Use of Proceeds*. The Company will use the net proceeds received by it from the sale of the Securities in all material respects in the manner specified in the Registration Statement, the General Disclosure Package and the Prospectus under “Use of Proceeds.”

(h) *Listing*. The Company will use its best efforts to effect and its reasonable best efforts to maintain the listing of the Common Stock (including the Securities) on the Nasdaq Global Market.

(i) *Restriction on Sale of Securities*. During a period of 180 days from the date of the Prospectus, the Company will not, without the prior written consent of Leerink, (i) directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock or file any registration statement under the 1933 Act with respect to any of the foregoing or (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the Common Stock, whether any such swap or transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or such other securities, in cash or otherwise. The foregoing sentence shall not apply to (A) the Securities to be sold hereunder, (B) any shares of Common Stock issued by the Company upon the exercise of an option or warrant or the conversion of a security outstanding on the date hereof and referred to in the Registration Statement, the General Disclosure Package and the Prospectus, (C) any shares of Common Stock issued or options to purchase Common Stock granted pursuant to employee benefit or stock incentive plans of the Company referred to in the Registration Statement, the General Disclosure Package and the Prospectus; (D) any shares of Common Stock issued pursuant to any non-employee director stock plan or dividend reinvestment plan referred to in the Registration Statement, the General Disclosure Package and the Prospectus; (E) the filing by the Company of any registration statement on Form S-8 or a successor form thereto or (F) shares of Common Stock or other securities issued in connection with a transaction that includes a commercial relationship (including joint ventures or other strategic acquisitions), provided that (x) the aggregate number of shares issued pursuant to this clause (F) shall not exceed 5.0% of the total number of outstanding shares of Common Stock immediately following the issuance and sale of the Securities at the Closing Time pursuant hereto and (y) the recipient of any such shares of Common Stock and securities issued pursuant to this clause (F) during the 180-day restricted period described above shall be subject to the restrictions set forth in a lock-up agreement described in Section 5(i) hereof for the remainder of such restricted period.

(j) If Leerink, in its sole discretion, agrees to release or waive the restrictions set forth in a lock-up agreement described in Section 5(i) hereof for an officer or director of the Company and provides the Company with notice of the impending release or waiver at least three business days before the effective date of the release or waiver, the Company agrees to announce the impending release or waiver by a press release substantially in the form of Exhibit C hereto through a major news service at least two business days before the effective date of the release or waiver.

(k) *Reporting Requirements*. The Company, during the period when a Prospectus relating to the Securities is (or, but for the exception afforded by Rule 172, would be) required to be delivered under the 1933 Act, will file all documents required to be filed with the Commission pursuant to the 1934 Act within the time periods required by the 1934 Act and 1934 Act Regulations. Additionally, the Company shall report the use of proceeds from the issuance of the Securities as may be required under Rule 463 under the 1933 Act.

(l) *Issuer Free Writing Prospectuses*. The Company agrees that, unless it obtains the prior written consent of the Representative, it will not make any offer relating to the Securities that would constitute an Issuer Free Writing Prospectus or that would otherwise constitute a “free writing prospectus,” or a portion thereof, required to be filed by the Company with the Commission or retained by the Company under Rule 433; provided that the Representative will be deemed to have consented to the Issuer Free Writing Prospectuses listed on Schedule B-2 hereto and any “road show that is a written communication” within the meaning of Rule 433(d)(8)(i) that has been reviewed by the Representative. The Company represents that it has treated or agrees that it will treat each such free writing prospectus consented to, or deemed consented to, by the Representative as an “issuer free writing prospectus,” as defined in Rule 433, and that it has complied and will comply with the applicable requirements of Rule 433 with respect thereto, including timely filing with the Commission where required, legending and record keeping. If at any time following issuance of an Issuer Free Writing Prospectus there occurred or occurs an event or development as a result of which such Issuer Free Writing Prospectus conflicted or would conflict with the information contained in the Registration Statement, any preliminary prospectus or the Prospectus or included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company will promptly notify the Representative and will promptly amend or supplement, at its own expense, such Issuer Free Writing Prospectus to eliminate or correct such conflict, untrue statement or omission.

(m) [INTENTIONALLY OMITTED]

(n) Testing-the-Waters Materials. If at any time following the distribution of any Written Testing-the-Waters Communication there occurred or occurs an event or development as a result of which such Written Testing-the-Waters Communication included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company will promptly notify the Representative and will promptly amend or supplement, at its own expense, such Written Testing-the-Waters Communication to eliminate or correct such untrue statement or omission.

(o) Emerging Growth Company Status. The Company will promptly notify the Representative if the Company ceases to be an Emerging Growth Company at any time prior to the later of (i) completion of the distribution of the Securities within the meaning of the 1933 Act and (ii) completion of the 180-day restricted period referred to in Section 3(i).

SECTION 4. Payment of Expenses.

(a) *Expenses*. The Company will pay or cause to be paid all expenses incident to the performance of its obligations under this Agreement, including (i) the preparation, printing and filing of the Registration Statement (including financial statements and exhibits) as originally filed and each amendment thereto, (ii) the preparation, printing and delivery to the Underwriters of copies of each preliminary prospectus, each Issuer Free Writing Prospectus and the Prospectus and any amendments or supplements thereto and any costs associated with electronic delivery of any of the foregoing by the Underwriters to investors, (iii) the preparation, issuance and delivery of the certificates for the Securities to the Underwriters, including any stock or other transfer taxes and any stamp or other duties payable upon the sale, issuance or delivery of the Securities to the Underwriters, (iv) the fees and disbursements of the Company's counsel, accountants and other advisors, (v) the qualification of the Securities under securities laws in accordance with the provisions of Section 3(e) hereof, including filing fees and the reasonable fees and disbursements of counsel for the Underwriters in connection therewith and in connection with the preparation of a "Blue Sky Survey" and any supplement thereto, (vi) the fees and expenses of any transfer agent or registrar for the Securities, (vii) the costs and expenses of the Company relating to investor presentations on any "road show" undertaken in connection with the marketing of the Securities, including without limitation, expenses associated with the production of road show slides and graphics, fees and expenses of any consultants engaged by the Company in connection with the road show presentations, travel and lodging expenses of the representatives and officers of the Company and any such consultants (provided that the travel, lodging and any car travel expenses of the representatives of the Underwriters shall be paid by the Underwriters), and 50 percent of and the cost of aircraft and other transportation chartered in connection with the road show, (viii) the filing fees incident to, and the reasonable fees and disbursements of counsel to the Underwriters in connection with, the review by FINRA of the terms of the sale of the Securities, (ix) the fees and expenses incurred in connection with the listing of the Securities on the Nasdaq Global Market, and (x) the costs and expenses (including, without limitation, any damages or other amounts payable in connection with legal or contractual liability) associated with the reforming of any contracts for sale of the Securities made by the Underwriters caused by a breach of the representation contained in the third sentence of Section 1(a)(ii).

(b) *Termination of Agreement*. If this Agreement is terminated by the Representative in accordance with the provisions of Section 5, Section 9(a)(i) or (iii) or Section 10 hereof, the Company shall reimburse the Underwriters for all of their reasonably documented out-of-pocket expenses, including the reasonable fees and disbursements of counsel for the Underwriters; provided, however, that if this Agreement is terminated by the Representative pursuant to Section 10, the Company shall have no obligation to reimburse any out-of-pocket expenses of the Underwriters that have failed to purchase the Securities that they have agreed to purchase hereunder.

SECTION 5. Conditions of Underwriters' Obligations. The obligations of the several Underwriters hereunder are subject to the accuracy of the representations and warranties of the Company contained herein or in certificates of any officer of the Company or its subsidiary delivered pursuant to the provisions hereof, to the performance by the Company of its covenants and other obligations hereunder, and to the following further conditions:

(a) *Effectiveness of Registration Statement; Rule 430A Information*. The Registration Statement, including any Rule 462(b) Registration Statement, has become effective and, at the Closing Time, no stop order suspending the effectiveness of the Registration Statement or any post-effective amendment thereto has been issued under the 1933 Act, no order preventing or suspending the use of any preliminary prospectus or the Prospectus has been issued and no proceedings for any of those purposes have been instituted or are pending or, to the Company's knowledge, contemplated; and the Company has complied with each request (if any) from the Commission for additional information. A prospectus containing the Rule 430A Information shall have been filed with the Commission in the manner and within the time frame required by Rule 424(b) without reliance on Rule 424(b)(8) or a post-effective amendment providing such information shall have been filed with, and declared effective by, the Commission in accordance with the requirements of Rule 430A.

(b) *Opinion of Counsel for Company*. At the Closing Time, the Representative shall have received the opinion, dated the Closing Time, of Wilmer Cutler Pickering Hale and Dorr LLP, counsel for the Company, together with the opinion of Lando & Anastasi, LLP, special counsel for the Company with respect to intellectual property, each in form and substance satisfactory to counsel for the Underwriters, together with signed or reproduced copies of such letter for each of the other Underwriters to the effect set forth in Exhibits A-1 and A-2 hereto.

(c) *Opinion of Counsel for Underwriters*. At the Closing Time, the Representative shall have received the opinion, dated the Closing Time, of Ropes & Gray LLP, counsel for the Underwriters, together with signed or reproduced copies of such letter for each of the other Underwriters with respect to such matters as the Representative may reasonably request. In giving such opinion such counsel may rely, as to all matters governed by the laws of jurisdictions other than the law of the State of New York, the General Corporation Law of the State of Delaware and the federal securities laws of the United States, upon the opinions of counsel satisfactory to the Representative. Such counsel may also state that, insofar as such opinion involves factual matters, they have relied, to the extent they deem proper, upon certificates of officers and other representatives of the Company and its subsidiary and certificates of public officials.

(d) *Officers' Certificate*. At the Closing Time, there shall not have been, since the date hereof or since the respective dates as of which information is given in the Registration Statement, the General Disclosure Package or the Prospectus, any material adverse change in the condition, financial or otherwise, or in the earnings, business affairs or business prospects of the Company and its subsidiary considered as one enterprise, whether or not arising in the ordinary course of business, and the Representative shall have received a certificate of the President and Chief Executive Officer of the Company and of the Senior Vice President and Chief Business Officer of the Company, dated the Closing Time, to the effect that (i) there has been no such Material Adverse Effect, (ii) the representations and warranties of the Company in this Agreement are true and correct with the same force and effect as though expressly made at and as of the Closing Time, (iii) the Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied at or prior to the Closing Time, and (iv) no stop order suspending the effectiveness of the Registration Statement under the 1933 Act has been issued, no order preventing or suspending the use of any preliminary prospectus or the Prospectus has been issued and no proceedings for any of those purposes have been instituted or are pending or, to their knowledge, contemplated.

(e) *Accountant's Comfort Letter*. At the time of the execution of this Agreement, the Representative shall have received from Deloitte & Touche LLP a letter, dated such date, in form and substance satisfactory to the Representative, together with signed or reproduced copies of such letter for each of the other Underwriters containing statements and information of the type ordinarily included in accountants' "comfort letters" to underwriters with respect to the financial statements and certain financial information contained in the Registration Statement, the General Disclosure Package and the Prospectus.

(f) *Bring-down Comfort Letter*. At the Closing Time, the Representative shall have received from Deloitte & Touche LLP a letter, dated as of the Closing Time, to the effect that they reaffirm the statements made in the letter furnished pursuant to subsection (e) of this Section, except that the specified date referred to shall be a date not more than three business days prior to the Closing Time.

(g) *Approval of Listing*. At the Closing Time, the Securities shall have been approved for listing on the Nasdaq Global Market, subject only to official notice of issuance.

(h) *No Objection*. FINRA has confirmed that it has not raised any objection with respect to the fairness and reasonableness of the underwriting terms and arrangements relating to the offering of the Securities.

(i) *Lock-up Agreements*. At the date of this Agreement, the Representative shall have received an agreement substantially in the form of Exhibit B hereto signed by the persons and entities listed on Schedule C hereto.

(j) *Conditions to Purchase of Option Securities*. In the event that the Underwriters exercise their option provided in Section 2(b) hereof to purchase all or any portion of the Option Securities, the representations and warranties of the Company contained herein and the statements in any certificates furnished by the Company and its subsidiary hereunder shall be true and correct as of each Date of Delivery and, at the relevant Date of Delivery, the Representative shall have received:

(i) Officers' Certificate. A certificate, dated such Date of Delivery, of the President and Chief Executive Officer of the Company and of the Senior Vice President and Chief Business Officer of the Company confirming that the certificate delivered at the Closing Time pursuant to Section 5(d) hereof remains true and correct as of such Date of Delivery.

(ii) Opinion of Counsel for Company. If requested by the Representative, the opinion of Wilmer Cutler Pickering Hale and Dorr LLP, counsel for the Company, together with the opinion of Lando & Anastasi, LLP, special counsel for the Company with respect to intellectual property, each in form and substance satisfactory to counsel for the Underwriters, dated such Date of Delivery, relating to the Option Securities to be purchased on such Date of Delivery and otherwise to the same effect as the opinion required by Section 5(b) hereof.

(iii) Opinion of Counsel for Underwriters. If requested by the Representative, the opinion of Ropes & Gray LLP, counsel for the Underwriters, dated such Date of Delivery, relating to the Option Securities to be purchased on such Date of Delivery and otherwise to the same effect as the opinion required by Section 5(c) hereof.

(iv) Bring-down Comfort Letter. If requested by the Representative, a letter from Deloitte & Touche LLP, in form and substance satisfactory to the Representative and dated such Date of Delivery, substantially in the same form and substance as the letter furnished to the Representative pursuant to Section 5(e) hereof, except that the "specified date" in the letter furnished pursuant to this paragraph shall be a date not more than three business days prior to such Date of Delivery.

(k) *Additional Documents*. At the Closing Time and at each Date of Delivery (if any) counsel for the Underwriters shall have been furnished with such documents and opinions as they may reasonably require for the purpose of enabling them to pass upon the issuance and sale of the Securities as herein contemplated, or in order to evidence the accuracy of any of the representations or warranties, or the fulfillment of any of the conditions, herein contained; and all proceedings taken by the Company in connection with the issuance and sale of the Securities as herein contemplated shall be reasonably satisfactory in form and substance to the Representative and counsel for the Underwriters.

(l) *Termination of Agreement*. If any condition specified in this Section shall not have been fulfilled when and as required to be fulfilled, this Agreement, or, in the case of any condition to the purchase of Option Securities on a Date of Delivery which is after the Closing Time, the obligations of the several Underwriters to purchase the relevant Option Securities, may be terminated by the Representative by notice to the Company at any time at or prior to Closing Time or such Date of Delivery, as the case may be, and such termination shall be without liability of any party to any other party except as provided in Section 4 and except that Sections 1, 6, 7, 8, 14, 15 and 16 shall survive any such termination and remain in full force and effect.

SECTION 6. Indemnification.

(a) *Indemnification of Underwriters*. The Company agrees to indemnify and hold harmless each Underwriter, its affiliates (as such term is defined in Rule 501(b) under the 1933 Act (each, an "Affiliate")), its selling agents and each person, if any, who controls any Underwriter within the meaning of Section 15 of the 1933 Act or Section 20 of the 1934 Act as follows:

(i) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, arising out of any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement (or any amendment thereto), including the Rule 430A Information, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading or arising out of any untrue statement or alleged untrue statement of a material fact included (A) in any preliminary prospectus, any Issuer Free Writing Prospectus, any Written Testing-the-Waters Communication, the General Disclosure Package or the Prospectus (or any amendment or supplement thereto), or (B) in any materials or information provided to investors by, or with the approval of, the Company in connection with the marketing of the offering of the Securities ("Marketing Materials"), including any roadshow or investor presentations made to investors by the Company (whether in person or electronically), or the omission or alleged omission in any preliminary prospectus, Issuer Free Writing Prospectus, any Written Testing-the-Waters Communication, Prospectus or in any Marketing Materials of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading;

(ii) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, to the extent of the aggregate amount paid in settlement of any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or of any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission; provided that (subject to Section 6(d) below) any such settlement is effected with the written consent of the Company;

(iii) against any and all expense whatsoever, as incurred (including the fees and disbursements of counsel chosen by Leerink), reasonably incurred in investigating, preparing or defending against any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission, to the extent that any such expense is not paid under (i) or (ii) above;

provided, however, that this indemnity agreement shall not apply to any loss, liability, claim, damage or expense to the extent arising out of any untrue statement or omission or alleged untrue statement or omission made in the Registration Statement (or any amendment thereto), including the Rule 430A Information, the General Disclosure Package or the Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with the Underwriter Information.

(b) *Indemnification of Company, Directors and Officers*. Each Underwriter severally agrees to indemnify and hold harmless the Company, its directors, each of its officers who signed the Registration Statement, and each person, if any, who controls the Company within the meaning of Section 15 of the 1933 Act or Section 20 of the 1934 Act, against any and all loss, liability, claim, damage and expense described in the indemnity contained in subsection (a) of this Section, as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions, made in the Registration Statement (or any amendment thereto), including the Rule 430A Information, the General Disclosure Package or the Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with the Underwriter Information.

(c) *Actions against Parties; Notification*. Each indemnified party shall give notice as promptly as reasonably practicable to each indemnifying party of any action commenced against it in respect of which indemnity may be sought hereunder, but failure to so notify an indemnifying party shall not relieve such indemnifying party from any liability hereunder to the extent it is not materially prejudiced as a result thereof and in any event shall not relieve it from any liability which it may have otherwise than on account of this indemnity agreement. In the case of parties indemnified pursuant to Section 6(a) above, counsel to the indemnified parties shall be selected by Leerink, and, in the case of parties indemnified pursuant to Section 6(b) above, counsel to the indemnified parties shall be selected by the Company. An indemnifying party may participate at its own expense in the defense of any such action; provided, however, that counsel to the indemnifying party shall not (except with the consent of the indemnified party) also be counsel to the indemnified party. In no event shall the indemnifying parties be liable for the reasonable fees and expenses of more than one counsel (in addition to any local counsel) separate from their own counsel for all indemnified parties in connection with any one action or separate but similar or related actions in the same jurisdiction arising out of the same general allegations or circumstances. No indemnifying party shall, without the prior written consent of the indemnified parties, settle or compromise or consent to the entry of any judgment with respect to any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or any claim whatsoever in respect of which indemnification or contribution could be sought under this Section 6 or Section 7 hereof (whether or not the indemnified parties are actual or potential parties thereto), unless such settlement, compromise or consent (i) includes an unconditional release of each indemnified party from all liability arising out of such litigation, investigation, proceeding or claim and (ii) does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any indemnified party.

(d) *Settlement without Consent if Failure to Reimburse*. If at any time an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for fees and expenses of counsel, such indemnifying party agrees that it shall be liable for any settlement of the nature contemplated by Section 6(a)(ii) effected without its written consent if (i) such settlement is entered into more than 60 days after receipt by such indemnifying party of the aforesaid request, (ii) such indemnifying party shall have received notice of the terms of such settlement at least 30 days prior to such settlement being entered into and (iii) such indemnifying party shall not have reimbursed such indemnified party in accordance with such request prior to the date of such settlement.

SECTION 7. Contribution. If the indemnification provided for in Section 6 hereof is for any reason unavailable to or insufficient to hold harmless an indemnified party in respect of any losses, liabilities, claims, damages or expenses referred to therein, then each indemnifying party shall contribute to the aggregate amount of such losses, liabilities, claims, damages and expenses incurred by such indemnified party, as incurred, (i) in such proportion as is appropriate to reflect the relative benefits received by the Company, on the one hand, and the Underwriters, on the other hand, from the offering of the Securities pursuant to this Agreement or (ii) if the allocation provided by clause (i) is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above but also the relative fault of the Company, on the one hand, and of the Underwriters, on the other hand, in connection with the statements or omissions which resulted in such losses, liabilities, claims, damages or expenses, as well as any other relevant equitable considerations.

The relative benefits received by the Company, on the one hand, and the Underwriters, on the other hand, in connection with the offering of the Securities pursuant to this Agreement shall be deemed to be in the same respective proportions as the total net proceeds from the offering of the Securities pursuant to this Agreement (before deducting expenses) received by the Company, on the one hand, and the total underwriting discount received by the Underwriters, on the other hand, in each case as set forth on the cover of the Prospectus, bear to the aggregate initial public offering price of the Securities as set forth on the cover of the Prospectus.

The relative fault of the Company, on the one hand, and the Underwriters, on the other hand, shall be determined by reference to, among other things, whether any such untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company or by the Underwriters and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

The Company and the Underwriters agree that it would not be just and equitable if contribution pursuant to this Section 7 were determined by pro rata allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation which does not take account of the equitable considerations referred to above in this Section 7. The aggregate amount of losses, liabilities, claims, damages and expenses incurred by an indemnified party and referred to above in this Section 7 shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in investigating, preparing or defending against any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or any claim whatsoever based upon any such untrue or alleged untrue statement or omission or alleged omission.

Notwithstanding the provisions of this Section 7, no Underwriter shall be required to contribute any amount in excess of the underwriting commissions received by such Underwriter in connection with the Securities underwritten by it and distributed to the public.

No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the 1933 Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation.

For purposes of this Section 7, each person, if any, who controls an Underwriter within the meaning of Section 15 of the 1933 Act or Section 20 of the 1934 Act and each Underwriter's Affiliates and selling agents shall have the same rights to contribution as such Underwriter, and each director of the Company, each officer of the Company who signed the Registration Statement, and each person, if any, who controls the Company within the meaning of Section 15 of the 1933 Act or Section 20 of the 1934 Act shall have the same rights to contribution as the Company. The Underwriters' respective obligations to contribute pursuant to this Section 7 are several in proportion to the number of Initial Securities set forth opposite their respective names in Schedule A hereto and not joint.

SECTION 8. Representations, Warranties and Agreements to Survive. All representations, warranties and agreements contained in this Agreement or in certificates of officers of the Company or its subsidiary submitted pursuant hereto, shall remain operative and in full force and effect regardless of (i) any investigation made by or on behalf of any Underwriter or its Affiliates or selling agents, any person controlling any Underwriter, its officers or directors or any person controlling the Company and (ii) delivery of and payment for the Securities.

SECTION 9. Termination of Agreement.

(a) *Termination*. The Representative may terminate this Agreement, by notice to the Company, at any time at or prior to the Closing Time (i) if there has been, in the judgment of the Representative, since the time of execution of this Agreement or since the respective dates as of which information is given in the Registration Statement, the General Disclosure Package or the Prospectus, any material adverse change in the condition, financial or otherwise, or in the earnings, business affairs or business prospects of the Company and its subsidiary considered as one enterprise, whether or not arising in the ordinary course of business, or (ii) if there has occurred any material adverse change in the financial markets in the United States or the international financial markets, any outbreak of hostilities or escalation thereof or other calamity or crisis or any change or development involving a prospective change in national or international political, financial or economic conditions, in each case the effect of which is such as to make it, in the judgment of the Representative, impracticable or inadvisable to proceed with the completion of the offering or to enforce contracts for the sale of the Securities, or (iii) if trading in any securities of the Company has been suspended or materially limited by the Commission or the Nasdaq Global Market, or (iv) if trading generally on the NYSE Amex or the New York Stock Exchange or in the Nasdaq Global Market has been suspended or materially limited, or minimum or maximum prices for trading have been fixed, or maximum ranges for prices have been required, by any of said exchanges or by order of the Commission, FINRA or any other governmental authority, or (v) a material disruption has occurred in commercial banking or securities settlement or clearance services in the United States or with respect to Clearstream or Euroclear systems in Europe, or (vi) if a banking moratorium has been declared by either Federal or New York authorities.

(b) *Liabilities*. If this Agreement is terminated pursuant to this Section, such termination shall be without liability of any party to any other party except as provided in Section 4 hereof, and provided further that Sections 1, 6, 7, 8, 14, 15 and 16 shall survive such termination and remain in full force and effect.

SECTION 10. Default by One or More of the Underwriters. If one or more of the Underwriters shall fail at the Closing Time or a Date of Delivery to purchase the Securities which it or they are obligated to purchase under this Agreement (the "Defaulted Securities"), the Representative shall have the right, within 24 hours thereafter, to make arrangements for one or more of the non-defaulting Underwriters, or any other underwriters, to purchase all, but not less than all, of the Defaulted Securities in such amounts as may be agreed upon and upon the terms herein set forth; if, however, the Representative shall not have completed such arrangements within such 24-hour period, then:

(i) if the number of Defaulted Securities does not exceed 10% of the number of Securities to be purchased on such date, each of the non-defaulting Underwriters shall be obligated, severally and not jointly, to purchase the full amount thereof in the proportions that their respective underwriting obligations hereunder bear to the underwriting obligations of all non-defaulting Underwriters, or

(ii) if the number of Defaulted Securities exceeds 10% of the number of Securities to be purchased on such date, this Agreement or, with respect to any Date of Delivery which occurs after the Closing Time, the obligation of the Underwriters to purchase, and the Company to sell, the Option Securities to be purchased and sold on such Date of Delivery shall terminate without liability on the part of any non-defaulting Underwriter.

No action taken pursuant to this Section shall relieve any defaulting Underwriter from liability in respect of its default.

In the event of any such default which does not result in a termination of this Agreement or, in the case of a Date of Delivery which is after the Closing Time, which does not result in a termination of the obligation of the Underwriters to purchase and the Company to sell the relevant Option Securities, as the case may be, either the (i) Representative or (ii) the Company shall have the right to postpone Closing Time or the relevant Date of Delivery, as the case may be, for a period not exceeding seven days in order to effect any required changes in the Registration Statement, the General Disclosure Package or the Prospectus or in any other documents or arrangements. As used herein, the term “Underwriter” includes any person substituted for an Underwriter under this Section 10.

SECTION 11. Notices. All notices and other communications hereunder shall be in writing and shall be deemed to have been duly given if mailed or transmitted by any standard form of telecommunication. Notices to the Underwriters shall be directed to Leerink Partners LLC, Attention: Syndicate Department, One Federal Street, 37th Floor, Boston, MA 02110, or by email at Syndicate@Leerink.com, or by phone at 800-808-7525; notices to the Company shall be directed to it at Cerulean Pharma Inc., 840 Memorial Drive, Cambridge, MA 02139, attention of Oliver S. Fetzer (facsimile: (617) 494-1544).

SECTION 12. No Advisory or Fiduciary Relationship. The Company acknowledges and agrees that (a) the purchase and sale of the Securities pursuant to this Agreement, including the determination of the initial public offering price of the Securities and any related discounts and commissions, is an arm’s-length commercial transaction between the Company, on the one hand, and the several Underwriters, on the other hand, (b) in connection with the offering of the Securities and the process leading thereto, each Underwriter is and has been acting solely as a principal and is not the agent or fiduciary of the Company, its subsidiary or their respective stockholders, creditors, employees or any other party, (c) no Underwriter has assumed or will assume an advisory or fiduciary responsibility in favor of the Company with respect to the offering of the Securities or the process leading thereto (irrespective of whether such Underwriter has advised or is currently advising the Company or its subsidiary on other matters) and no Underwriter has any obligation to the Company with respect to the offering of the Securities except the obligations expressly set forth in this Agreement, (d) the Underwriters and their respective affiliates may be engaged in a broad range of transactions that involve interests that differ from those of the Company and (e) the Underwriters have not provided any legal, accounting, regulatory or tax advice with respect to the offering of the Securities and the Company has consulted its own respective legal, accounting, regulatory and tax advisors to the extent it deemed appropriate.

SECTION 13. Parties. This Agreement shall each inure to the benefit of and be binding upon the Underwriters and the Company and their respective successors. Nothing expressed or mentioned in this Agreement is intended or shall be construed to give any person, firm or corporation, other than the Underwriters and the Company and their respective successors and the controlling persons and officers and directors referred to in Sections 6 and 7 and their heirs and legal representatives, any legal or equitable right, remedy or claim under or in respect of this Agreement or any provision herein contained. This Agreement and all conditions and provisions hereof are intended to be for the sole and exclusive benefit of the Underwriters and the Company and their respective successors, and said controlling persons and officers and directors and their heirs and legal representatives, and for the benefit of no other person, firm or corporation. No purchaser of Securities from any Underwriter shall be deemed to be a successor by reason merely of such purchase.

SECTION 14. Trial by Jury. The Company (on its behalf and, to the extent permitted by applicable law, on behalf of its stockholders and affiliates) and each of the Underwriters hereby irrevocably waives, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to this Agreement or the transactions contemplated hereby.

SECTION 15. GOVERNING LAW. THIS AGREEMENT AND ANY CLAIM, CONTROVERSY OR DISPUTE ARISING UNDER OR RELATED TO THIS AGREEMENT SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF, THE STATE OF NEW YORK WITHOUT REGARD TO ITS CHOICE OF LAW PROVISIONS.

SECTION 16. Consent to Jurisdiction; Waiver of Immunity. Any legal suit, action or proceeding arising out of or based upon this Agreement or the transactions contemplated hereby shall be instituted in (i) the federal courts of the United States of America located in the City and County of New York, Borough of Manhattan or (ii) the courts of the State of New York located in the City and County of New York, Borough of Manhattan (collectively, the "Specified Courts"), and each party irrevocably submits to the exclusive jurisdiction (except for proceedings instituted in regard to the enforcement of a judgment of any such court, as to which such jurisdiction is non-exclusive) of such courts in any such suit, action or proceeding. Service of any process, summons, notice or document by mail to such party's address set forth above shall be effective service of process for any suit, action or other proceeding brought in any such court. The parties irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the Specified Courts and irrevocably and unconditionally waive and agree not to plead or claim in any such court that any such suit, action or other proceeding brought in any such court has been brought in an inconvenient forum.

SECTION 17. TIME. TIME SHALL BE OF THE ESSENCE OF THIS AGREEMENT. EXCEPT AS OTHERWISE SET FORTH HEREIN, SPECIFIED TIMES OF DAY REFER TO NEW YORK CITY TIME.

SECTION 18. Counterparts. This Agreement may be executed in any number of counterparts, each of which shall be deemed to be an original, but all such counterparts shall together constitute one and the same agreement.

SECTION 19. Effect of Headings. The Section headings herein are for convenience only and shall not affect the construction hereof.

(Signature page follows)

If the foregoing is in accordance with your understanding of our agreement, please sign and return to the Company a counterpart hereof, whereupon this instrument, along with all counterparts, will become a binding agreement among the Underwriters and the Company in accordance with its terms.

Very truly yours,

CERULEAN PHARMA INC.

By ______________________________
Name:
Title:

CONFIRMED AND ACCEPTED,
as of the date first above written:

LEERINK PARTNERS LLC

By ______________________________
Name:
Title:

For themselves and as Representative of the other Underwriters named in Schedule A hereto.

Signature Page to Underwriting Agreement

SCHEDULE A

The initial public offering price per share for the Securities shall be $[—].

The purchase price per share for the Securities to be paid by the several Underwriters shall be $[—], being an amount equal to the initial public offering price set forth above less $[—] per share, subject to adjustment in accordance with Section 2(b) for dividends or distributions declared by the Company and payable on the Initial Securities but not payable on the Option Securities.

Name of Underwriter	Number of Initial Securities
Leerink Partners LLC	
Canaccord Genuity Inc.	
JMP Securities LLC	
Wedbush Securities Inc.	
Total	

SCHEDULE B-1

Pricing Terms

1. The Company is selling [—] shares of Common Stock.

2. The Company has granted an option to the Underwriters, severally and not jointly, to purchase up to an additional [—] shares of Common Stock.

3. The initial public offering price per share for the Securities shall be $[—].

SCHEDULE B-2

Free Writing Prospectuses

[—]

SCHEDULE B-3

Written Testing-the-Waters Communications

[—]

SCHEDULE C

List of Persons and Entities Subject to Lock-up

[—]

Exhibit A

FORM OF OPINION OF COMPANY’S COUNSEL TO BE DELIVERED PURSUANT TO SECTION 5(b)

[—]

Exhibit B

Form of Lock-Up Agreement

, 2014

Leerink Partners LLC
as Representative of the several Underwriters

c/o Leerink Partners LLC
One Federal Street, Floor 37
Boston, MA 02110

Re: Proposed Public Offering by Cerulean Pharma Inc.

Ladies and Gentlemen:

The undersigned, a stockholder, officer and/or director of Cerulean Pharma Inc., a Delaware corporation (the "Company"), understands that Leerink Partners LLC ("Leerink") proposes to enter into an Underwriting Agreement (the "Underwriting Agreement") with the Company providing for the public offering (the "Public Offering") of shares (the "Securities") of the Company's common stock, par value $0.0001 per share (the "Common Stock"). In recognition of the benefit that such an offering will confer upon the undersigned as a stockholder, an officer and/or a director of the Company, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the undersigned agrees with each underwriter to be named in the Underwriting Agreement (collectively, the "Underwriters") that, during the period beginning on the date hereof and ending on the date that is 180 days from the date of the Underwriting Agreement (the "Lock-Up Period"), the undersigned will not, without the prior written consent of Leerink, directly or indirectly, (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant for the sale of, or otherwise dispose of or transfer any shares of the Company's Common Stock or any securities convertible into or exchangeable or exercisable for Common Stock, whether now owned or hereafter acquired by the undersigned or with respect to which the undersigned has or hereafter acquires the power of disposition (collectively, the "Lock-Up Securities"), or exercise any right with respect to the registration of any of the Lock-up Securities, or file or cause to be filed any registration statement in connection therewith (other than a Registration Statement on Form S-8), under the Securities Act of 1933, as amended, or (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the Lock-Up Securities, whether any such swap or transaction is to be settled by delivery of Common Stock or other securities, in cash or otherwise. If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed Securities the undersigned may purchase in the Public Offering.

If the undersigned is an officer or director of the Company, (1) Leerink agrees that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of shares of the Common Stock, Leerink will notify the Company of the impending release or waiver, and (2) the Company has agreed in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver. Any release or waiver granted by Leerink hereunder to any such officer or director shall only be effective two business days after the publication date of such press release. The provisions of this paragraph will not apply if (i) the release or waiver is effected solely to permit a transfer not for consideration and (ii) the transferee has agreed in writing to be bound by the same terms described in this letter to the extent and for the duration that such terms remain in effect at the time of the transfer.

Notwithstanding the foregoing, and subject to the conditions below, the undersigned may transfer the Lock-Up Securities without the prior written consent of Leerink, provided that (1) Leerink receives a signed lock-up agreement for the balance of the Lock-Up Period from each donee, trustee, distributee, or transferee, as the case may be, (2) any such transfer shall not involve a disposition for value, (3) in the case of clauses (i) through (v) below, such transfers are not required to be reported with the Securities and Exchange Commission on Form 4 in accordance with Section 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and (4) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers:

(i) as a *bona fide* gift or gifts; or

(ii) to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned (for purposes of this lock-up agreement, "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin); or

(iii) as a distribution to limited partners, members or stockholders or other equity holders of the undersigned; or

(iv) to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by the undersigned or the immediate family members of the undersigned; or

(v) to the undersigned's affiliates or to any investment fund or other entity controlled or managed by the undersigned; or

(vi) pursuant to a qualified domestic relations order or in connection with a divorce settlement; or

(vii) by will or intestate succession upon the death of the undersigned.

Furthermore, during the Lock-Up Period, the undersigned may (a) sell shares of Common Stock of the Company purchased by the undersigned in the Public Offering (provided that such shares of Common Stock shall not include any shares purchased by the undersigned through any directed share program established in connection with the Public Offering and except as provided in the last sentence of the first paragraph of this agreement) or on the open market following the Public Offering if and only if (i) such sales are not required during the Lock-Up Period to be reported in any press release or public report or filing with the Securities and Exchange Commission, or otherwise and (ii) the undersigned does not otherwise voluntarily effect any press release, public filing or report regarding such sales during the Lock-Up Period and (b) exercise an option to purchase shares of Common Stock granted under any of the Company's equity incentive plans existing as of the date of the Underwriting Agreement, or a warrant or other security existing as of the date of the Underwriting Agreement for shares of Common Stock, if and only if the shares of Common Stock received upon such exercise shall remain subject to the terms of this lock-up agreement.

In addition, the restrictions on transfer and disposition of the Lock-Up Securities during the Lock-Up Period shall not apply to the repurchase of Lock-Up Securities by the Company in connection with the termination of the undersigned's employment or other service with the Company.

In the event that Leerink releases, in full or in part, any officer, director or equity holder of the Company (a “Stockholder”) from the restrictions of any lock-up agreement signed by such Stockholder with the Underwriters (a “Triggering Release”), then the undersigned shall be released in the same manner from the restrictions of this agreement (i.e., in an amount equal to the same percentage of the shares of Common Stock being released in the Triggering Release relative to the undersigned’s ownership of Common Stock at the time of the request of the Triggering Release); provided that (i) in order to request a Triggering Release, the Stockholder requesting the Triggering Release must make a request in writing to the Company setting forth the number of shares of Common Stock to be released; (ii) the Company must notify the other Stockholders of the requested Triggering Release within three business days; (iii) any other Stockholder that intends to request a release of a pro rata portion of the shares of Common Stock held by them (the “Pro Rata Stockholders”) must (x) make such a request in writing to the Company and (y) certify in writing to the Underwriters and the Company the total number of shares of Common Stock held by such Pro Rata Stockholder; (iv) the Company must (x) make a request in writing to Leerink setting forth for the Stockholder requesting the Triggering Release and for each Pro Rata Stockholder the number of shares of Common Stock for which each such Stockholder is requesting a release and (y) provide to Leerink the total number of shares of common stock of the Company outstanding as of the date of the request of such Triggering Release and certify in writing to the Underwriters that such number is true and accurate. If the Company fails to notify the undersigned within three business days of the request of the Triggering Release, the failure to give such notice shall not give rise to any claim or liability against Leerink or the Underwriters.

Notwithstanding the foregoing, (i) no release by Leerink of any shares of Common Stock will constitute a Triggering Release if the aggregate of such releases granted to any individual Stockholder requesting a release does not exceed an aggregate amount of $250,000 of shares of Common Stock during the Lock-Up Period (for the avoidance of doubt, each individual affiliate of the undersigned that is a party to a separate lock-up agreement with the Underwriters shall be treated as a separate Stockholder); (ii) if the release, in full or in part, of any shares of Common Stock from the restrictions of its lock-up agreement is in connection with a follow-on offering of common stock (the “Follow-On Offering”), then the shares of Common Stock held by the undersigned shall be released only if the undersigned enters into a new lock-up agreement with the Underwriters with respect to the shares of Common Stock that are not being released, upon terms and conditions reasonably satisfactory to the Underwriters but with restrictions that will be no more restrictive than those set forth herein and only to the extent that the undersigned agrees to participate as a selling stockholder in the Follow-On Offering and to sell any of the shares of Common Stock released from the restrictions of this agreement in such Follow-On Offering; and (iii) Leerink shall not release, in full or in part, any Stockholder from the restrictions of any lock-up agreement signed by such Stockholder with the Underwriters unless such Stockholder shall have first made a request pursuant to the clause (i) of the preceding paragraph.

Notwithstanding anything herein to the contrary, nothing herein shall prevent the undersigned from establishing a trading plan that complies with Rule 10b5-l under the Exchange Act (“10b5-l Trading Plan”) or from amending an existing 10b5-l Trading Plan so long as in either case there are no sales of Lock-Up Securities under such plans during the Lock-Up Period; and provided that, the establishment of a 10b5-1 Trading Plan or the amendment of a 10b5-l Trading Plan shall only be permitted if (i) the establishment or amendment of such plan is not required to be reported in any public report or filing with the Securities and Exchange Commission, or otherwise and (ii) the undersigned does not otherwise voluntarily effect any public filing or report regarding the establishment or amendment of such plan.

The undersigned also agrees and consents to the entry of stop transfer instructions with the Company’s transfer agent and registrar against the transfer of the Lock-Up Securities except in compliance with the foregoing restrictions. This lock-up agreement shall automatically terminate, and the undersigned shall be released from its obligations hereunder, upon the earliest to occur, if any, of (i) prior to the execution of the Underwriting Agreement, the Company advises Leerink in writing that it has determined not to proceed with the Public Offering, (ii) the Company files an application to withdraw the registration statement related to the Public Offering, (iii) the Underwriting Agreement is executed but is terminated prior to the closing of the Public Offering (other than the provisions thereof which survive termination), or (iv) July 31, 2014, in the event that the Underwriting Agreement has not been executed by such date.

Very truly yours,

Signature: ________________________________
Print Name: ________________________________

Exhibit C

FORM OF PRESS RELEASE
TO BE ISSUED PURSUANT TO SECTION 3(j)

[—**]**

Exhibit 3.1

AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

(Pursuant to Sections 242 and 245 of the
General Corporation Law of the State of Delaware)

Cerulean Pharma Inc., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"),

DOES HEREBY CERTIFY:

1. That the name of this corporation is Cerulean Pharma Inc. (the "Corporation"), and that the Corporation was originally incorporated pursuant to the General Corporation Law on November 28, 2005 under the name Tempo Pharmaceuticals, Inc. The original Certificate of Incorporation of the Corporation was amended on each of December 1, 2005, October 20, 2006, December 22, 2006, May 8, 2007, December 6, 2007, October 14, 2008, July 9, 2009, July 13, 2009, May 26, 2010, November 12, 2010 and December 2, 2011.

2. That the Board of Directors duly adopted resolutions proposing to amend and restate the Certificate of Incorporation of the Corporation, as amended, declaring said amendment and restatement to be advisable and in the best interests of the Corporation and its stockholders, and authorizing the appropriate officers of the Corporation to solicit the consent of the stockholders therefor, which resolution setting forth the proposed amendment and restatement is as follows:

RESOLVED, that the Certificate of Incorporation, as amended, of the Corporation be amended and restated in its entirety to read as follows:

FIRST: The name of the Corporation is Cerulean Pharma Inc.

SECOND: The registered office of the Corporation in the State of Delaware is located at 2711 Centerville Road, Suite 400, in the City of Wilmington, County of New Castle 19808. The name of its registered agent at such address is Corporation Service Company.

THIRD: The purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law.

FOURTH: The number of authorized shares of each class or series of stock of the Corporation, and the powers, preferences and rights, and the qualifications, limitations or restrictions thereof, shall be as follows:

Section 1. CAPITAL STOCK

The total number of shares of all classes of stock which the Corporation shall have authority to issue is 220,894,772 shares consisting of 132,000,000 shares of common stock, $0.0001 par value per share (the "Common Stock"), and 88,894,772 shares of preferred stock, $0.01 par value per share (the "Preferred Stock").

Section 2. COMMON STOCK

2.1. Voting Rights. The holders of shares of Common Stock shall be entitled to one vote for each share so held with respect to all matters voted on by the stockholders of the Corporation, subject in all cases to Sections 3.4 and 3.6 of this Article Fourth.

Except as otherwise provided in the Corporation's Certificate of Incorporation, the number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of shares of stock of the Corporation representing a majority of the votes represented by all outstanding shares of stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of Delaware.

2.2. Liquidation Right. Subject to the prior and superior right of the Preferred Stock, upon any voluntary or involuntary liquidation, dissolution or winding up of the affairs of the Corporation, the holders of Common Stock shall be entitled to receive that portion of the remaining funds to be distributed to holders of Common Stock, subject to and as provided in Section 3.2 of this Article Fourth.

2.3. Dividends. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor as, when and if declared by the Board of Directors subject to any preferential dividend rights of any then outstanding Preferred Stock, including as provided in Section 3.5 of this Article Fourth.

Section 3. PREFERRED STOCK

3.1. Designation. Of the 88,894,772 shares of Preferred Stock, two million five hundred thousand (2,500,000) shares have been designated as Seed Convertible Preferred Stock (the "Seed Preferred Stock"), nine million three hundred seven thousand six hundred ninety two (9,307,692) shares have been designated Series A Convertible Preferred Stock (the "Series A Preferred Stock"), four million seventy seven thousand five hundred (4,077,500) shares have been designated Series B Convertible Preferred Stock (the "Series B Preferred Stock"), five million (5,000,000) shares have been designated Series B-1 Convertible Preferred Stock (the "Series B-1 Preferred Stock"), thirty three million three hundred ten thousand seven hundred eighty seven (33,310,787) shares have been designated Series C Convertible Preferred Stock (the "Series C Preferred Stock") and thirty four million six hundred ninety eight thousand seven hundred and ninety three (34,698,793) shares are hereby designated Series D Convertible Preferred Stock (the "Series D Preferred Stock").

3.2. Liquidation Rights.

(a) In the event of any Liquidating Event (as defined below), each holder of a share of Preferred Stock shall be entitled to receive, prior and in preference to any distribution of any of the assets or surplus funds of the Corporation to the holders of Common Stock by reason of their ownership thereof, an amount per share of Seed Preferred Stock equal to the Seed Original Issue Price (as defined below), an amount per share of Series A Preferred Stock equal to the Series A Original Issue Price (as defined below), an amount per share of Series B Preferred Stock equal to the Series B Original Issue Price (as defined below), an amount per share of Series B-1 Preferred Stock equal to the Series B-1 Original Issue Price (as defined below), an amount per share of Series C Preferred Stock equal to the Series C Original Issue Price (as defined below), and an amount per share of Series D Preferred Stock equal to the Series D Original Issue Price (as defined below), plus an amount equal to any declared but unpaid dividends thereon to and including the date full payment shall be tendered to the holders of the Preferred Stock with respect to such liquidation, dissolution or winding up (the amounts payable pursuant to this sentence are hereinafter referred to as the “Seed Liquidation Amount,” the “Series A Liquidation Amount,” the “Series B Liquidation Amount,” the “Series B-1 Liquidation Amount,” the “Series C Liquidation Amount” and the “Series D Liquidation Amount” respectively, and collectively, the “Liquidation Amounts”).

(b) If the assets or surplus funds to be distributed to the holders of the Preferred Stock pursuant to Section 3.2(a) are insufficient to permit the payment to such holders of their full Liquidation Amounts, the assets and surplus funds legally available for distribution shall be distributed ratably among the holders of the Preferred Stock in proportion to the full Liquidation Amount each such holder is otherwise entitled to receive under Section 3.2(a).

(c) All of the Liquidation Amounts to be paid to the holders of the Preferred Stock pursuant to this Section 3.2 in the event of a Liquidating Event shall be paid or set apart for payment before the payment or setting apart for payment of any amount for, or the distribution of any assets of the Corporation to, the holders of the Common Stock in connection with such Liquidating Event. Subject to the provisions of Section 3.2(d) below, after payment or the setting apart of payment to the holders of the Preferred Stock of the Liquidation Amounts so payable to them, all remaining assets available for distribution (after payment or provision for payment of all debts and liabilities of the Corporation) shall be distributed to the holders of the Common Stock and the Preferred Stock ratably in proportion to the number of shares of Common Stock they then hold, determined for this purpose as if each share of Preferred Stock had been converted voluntarily into Common Stock at the then-applicable Conversion Price (as defined below) immediately prior to such Liquidating Event, provided that no holder of any share of Preferred Stock shall receive any payment under this sentence of Section 3.2(c) with respect to such share to the extent that the aggregate of all payments with respect to such share under Section 3.2(a) and this sentence of Section 3.2(c) exceeds the product of two times the Liquidation Amount for such share of Preferred Stock.

(d) Notwithstanding anything in this Section 3.2 to the contrary, if a holder of any share of Preferred Stock would receive a greater amount pursuant to this Section 3.2 with respect to such share of Preferred Stock upon a Liquidating Event by voluntarily converting such share into Common Stock immediately prior to such Liquidating Event at the then-applicable

Conversion Price than such holder would be entitled to receive with respect to such share of Preferred Stock pursuant to this Section 3.2, then such holder shall not receive any Liquidation Amount with respect to such share under such Section 3.2(a), but shall be treated, for the purposes of determining such holder's rights with respect to such share under Sections 3.2(a) and 3.2(c) only, as though such holder had converted such share of Preferred Stock into Common Stock, effective immediately prior to the applicable Liquidating Event, at the then-applicable Conversion Price.

(e) A "Liquidating Event" shall mean (1) a liquidation, dissolution or winding up of the Corporation, either voluntary or involuntary, (2) a merger or consolidation in which either (I) the Corporation is a constituent party or (II) a subsidiary of the Corporation is a constituent party and the Corporation issues shares of its capital stock pursuant to such merger or consolidation, except any such merger or consolidation involving the Corporation or a subsidiary in which the shares of capital stock of the Corporation outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital stock that represent, immediately following such merger or consolidation, at least a majority, by voting power, of the capital stock of (i) the surviving or resulting corporation or (ii) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such merger or consolidation, the parent corporation of such surviving or resulting corporation, or (3) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Corporation or any subsidiary of the Corporation of all or substantially all the assets of the Corporation and its subsidiaries taken as a whole, or the sale or disposition (whether by merger or otherwise) of one or more subsidiaries of the Corporation if substantially all of the assets of the Corporation and its subsidiaries taken as a whole are held by such subsidiary or subsidiaries, except where such sale, lease, transfer, exclusive license or other disposition is to a wholly owned subsidiary of the Corporation; provided, however, that such a transaction shall not be regarded as a Liquidating Event and, to the extent applicable, all outstanding shares of Preferred Stock shall be treated under the provisions of Section 3.3(d)(vii) in lieu of this Section 3.2 in connection with such sale, merger or consolidation in the event that the holders of at least fifty-eight percent (58%) in voting power of the outstanding shares of Preferred Stock so elect, by written notice to the Corporation no later than fifteen (15) days before the effective date of such event.

(f) The Corporation shall not have the power to effect a Liquidating Event referred to in Section 3.2(e)(2)(I) unless the agreement or plan of merger or consolidation for such transaction (the "Merger Agreement") provides that the consideration payable to the stockholders of the Corporation shall be allocated among the holders of capital stock of the Corporation in accordance with this Section 3.2.

(g) In the event of a Liquidating Event referred to in Subsection 3.2(e)(2)(II) or 3.2(e)(3), if the Corporation does not effect a dissolution of the Corporation under the Delaware General Corporation Law within 90 days after such Liquidating Event, then (i) the Corporation shall send a written notice to each holder of Preferred Stock no later than the 90th day after the Liquidating Event advising such holders of their right (and the requirements to be met to secure such right) pursuant to the terms of the following clause (ii) to require the redemption of such shares of Preferred Stock, and (ii) if the holders of at least fifty-eight percent (58%) in voting power of the then-outstanding shares of Preferred Stock so request in a written instrument delivered to the Corporation not later than 30 days after receipt of such written notice from the Corporation, the Corporation shall use the consideration received by the Corporation for such Liquidating Event (net of any retained liabilities associated with the assets sold or technology licensed, as determined in good faith by the Board of Directors of the Corporation), together with any other assets of the Corporation available for distribution to its stockholders (the "Available Proceeds"), to the extent legally available therefor, on the 150th day after such Liquidating Event, to redeem all outstanding shares of Preferred Stock at a price per share equal to the amounts per share that each holder would be entitled to receive under this Section 3.2 upon a Liquidating Event in which the Available Proceeds were the amount available to the stockholders of the Corporation. Notwithstanding the foregoing, in the event of a redemption pursuant to the preceding sentence, if the Available Proceeds are not sufficient to redeem all outstanding shares of Preferred Stock, the Corporation shall redeem a pro rata portion of each holder's shares of Preferred Stock to the fullest extent of such Available Proceeds, based on the respective amounts which would otherwise be payable in respect of the shares to be redeemed if the Available Proceeds were sufficient to redeem all such shares, and shall redeem the remaining shares to have been redeemed as soon as practicable after the Corporation has funds legally available therefor. The provisions of Section 3.7 shall apply, with such necessary changes in the details thereof as are necessitated by the context, to the redemption of the Preferred Stock pursuant to this Section 3.2(g). Prior to the distribution or redemption provided for in this Section 3.2(g), the Corporation shall not expend or dissipate the consideration received for such Liquidating Event, except to discharge expenses incurred in connection with such Liquidating Event.

(h) In the event of a Liquidating Event pursuant to Section 3.2(e)(2)(I), if any portion of the consideration payable to the stockholders of the Corporation is placed into escrow and/or is payable to the stockholders of the Corporation subject to contingencies, the Merger Agreement shall provide that (a) the portion of such consideration that is not placed in escrow and not subject to any contingencies (the "Initial Consideration") shall be allocated among the holders of capital stock of the Corporation in accordance with this Section 3.2 as if the Initial Consideration were the only consideration payable in connection with such Liquidating Event and (b) any additional consideration which becomes payable to the stockholders of the Corporation upon release from escrow or satisfaction of contingencies shall be allocated among the holders of capital stock of the Corporation in accordance with this Section 3.2 after taking into account the previous payment of the Initial Consideration as part of the same transaction.

3.3. Conversion. The holders of Preferred Stock shall have conversion rights as follows (the "Conversion Rights"):

(a) Right to Convert.

(i) Each share of Seed Preferred Stock shall be convertible at the option of the holder thereof at any time after the date of issuance and without the payment of any additional consideration therefor into that number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Seed Original Issue Price (as defined below) by the Seed Conversion Price (as defined below) as adjusted pursuant to this Section 3.3 and in effect at the time of conversion. The "Seed Original Issue Price" shall mean $0.80 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares. Effective as of the Second Series D Original Issue Date (as defined below) and following the issuance of the Series D Preferred Stock at the Closing, as defined in that certain Second Series D Preferred Stock Purchase Agreement, dated on or about November 30, 2012, by and among the Corporation and the purchasers of shares of Series D Preferred Stock pursuant thereto (the "Second Series D Purchase Agreement"), the conversion price for the Seed Preferred Stock (the "Seed Conversion Price") is $0.76. The Seed Conversion Price shall be subject to adjustment after the Second Series D Original Issue Date (in order to adjust the number of shares of Common Stock into which the Seed Preferred Stock is convertible) as hereinafter provided. Each person so converting shares of Seed Preferred Stock shall be entitled to all declared but unpaid dividends up to the time of the conversion. Such dividends shall be paid to each such person within thirty (30) days of the date of conversion.

(ii) Each share of Series A Preferred Stock shall be convertible at the option of the holder thereof, at any time after the date of issuance and without the payment of any additional consideration therefor into that number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series A Original Issue Price (as defined below) by the Series A Conversion Price (as defined below) as adjusted pursuant to this Section 3.3 and in effect at the time of the conversion. The "Series A Original Issue Price" shall mean $1.30 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares. Effective as of the Second Series D Original Issue Date and following the issuance of the Series D Preferred Stock at the Closing, as defined in the Second Series D Purchase Agreement, the conversion price for the Series A Preferred Stock (the "Series A Conversion Price") is $0.97. The Series A Conversion Price shall be subject to adjustment after the Second Series D Original Issue Date (in order to adjust the number of shares of Common Stock into which the Series A Preferred Stock is convertible) as hereinafter provided. Each person so converting shares of Series A Preferred Stock shall be entitled to all declared but unpaid dividends up to the time of the conversion. Such dividends shall be paid to each person within thirty (30) days of the date of conversion.

(iii) Each share of Series B Preferred Stock shall be convertible at the option of the holder thereof, at any time after the date of issuance and without the payment of any additional consideration therefor into that number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series B Original Issue Price (as defined below) by the Series B Conversion Price (as defined below) as adjusted pursuant to this Section 3.3 and in effect at the time of the conversion. The "Series B Original Issue Price" shall mean $2.00 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares. Effective as of the Second Series D Original Issue Date and following the issuance of the Series D Preferred Stock at the Closing, as defined in the Second Series D Purchase Agreement, the conversion price for the Series B Preferred Stock (the "Series B Conversion Price") is $1.22. The Series B Conversion Price shall be subject to adjustment after the Second Series D Original Issue Date (in order to adjust the number of shares of Common Stock into which the Series B Preferred Stock is convertible) as hereinafter provided. Each person so converting shares of Series B Preferred Stock shall be entitled to all declared but unpaid dividends up to the time of the conversion. Such dividends shall be paid to each person within thirty (30) days of the date of conversion.

(iv) Each share of Series B-1 Preferred Stock shall be convertible at the option of the holder thereof, at any time after the date of issuance and without the payment of any additional consideration therefor into that number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series B-1 Original Issue Price (as defined below) by the Series B-1 Conversion Price (as defined below) as adjusted pursuant to this Section 3.3 and in effect at the time of the conversion. The "Series B-1 Original Issue Price" shall mean $2.00 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares. Effective as of the Second Series D Original Issue Date and following the issuance of the Series D Preferred Stock at the Closing, as defined in the Second Series D Purchase Agreement, the conversion price for the Series B-1 Preferred Stock (the "Series B-1 Conversion Price") is $0.74. The Series B-1 Conversion Price shall be subject to adjustment after the Second Series D Original Issue Date (in order to adjust the number of shares of Common Stock into which the Series B-1 Preferred Stock is convertible) as hereinafter provided. Each person so converting shares of Series B-1 Preferred Stock shall be entitled to all declared but unpaid dividends up to the time of the conversion. Such dividends shall be paid to each person within thirty (30) days of the date of conversion.

(v) Each share of Series C Preferred Stock shall be convertible at the option of the holder thereof, at any time after the date of issuance and without the payment of any additional consideration therefor into that number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series C Original Issue Price (as defined below) by the Series C Conversion Price (as defined below) as adjusted pursuant to this Section 3.3 and in effect at the time of the conversion. The "Series C Original Issue Price" shall mean $0.74 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares. Effective as of the Second Series D Original Issue Date and following the issuance of the Series D Preferred Stock at the Closing, as defined in the Second Series D Purchase Agreement, the conversion price for the Series C Preferred Stock (the "Series C Conversion Price") is $0.74. The Series C Conversion Price shall be subject to adjustment after the Second Series D Original Issue Date (in order to adjust the number of shares of Common Stock into which the Series C Preferred Stock is convertible) as hereinafter provided. Each person so converting shares of Series C Preferred Stock shall be entitled to all declared but unpaid dividends up to the time of the conversion. Such dividends shall be paid to each person within thirty (30) days of the date of conversion.

(vi) Each share of Series D Preferred Stock shall be convertible at the option of the holder thereof, at any time after the date of issuance and without the payment of any additional consideration therefor into that number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series D Original Issue Price (as defined below) by the Series D Conversion Price (as defined below) as adjusted pursuant to this Section 3.3 and in effect at the time of the conversion. The "Series D Original Issue Price" shall mean $0.83 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares. Effective as of the Second Series D Original Issue Date and following the issuance of the Series D Preferred Stock at the Closing, as defined in the Second Series D Purchase Agreement, the conversion price for the Series D Preferred Stock (the "Series D Conversion Price" and together with the Seed Conversion Price, the Series A Conversion Price, the Series B Conversion Price, the Series B-1

Conversion Price and the Series C Conversion Price, each a “Conversion Price” and together, the “Conversion Prices”) is $0.83. The Series D Conversion Price shall be subject to adjustment after the Second Series D Original Issue Date (in order to adjust the number of shares of Common Stock into which the Series D Preferred Stock is convertible) as hereinafter provided. Each person so converting shares of Series D Preferred Stock shall be entitled to all declared but unpaid dividends up to the time of the conversion. Such dividends shall be paid to each person within thirty (30) days of the date of conversion.

(b) Automatic Conversion. Each share of Preferred Stock shall automatically be converted into shares of Common Stock at the then-effective applicable Conversion Price upon:

(i) the closing of a firm commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the “Securities Act”), covering the offer and sale of Common Stock for the account of the Corporation to the public at a price of at least $2.50 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock), resulting in at least $30,000,000 of gross proceeds to the Corporation (a “Qualified IPO”); or

(ii) the written consent of holders in interest of at least fifty-eight percent (58%) in voting power of the Preferred Stock outstanding at that time.

The person(s) entitled to receive Common Stock issuable upon a conversion of Preferred Stock hereunder shall not be deemed to have converted the Preferred Stock until immediately prior to the closing of such offering or the receipt by the Corporation of such consent. Each person who holds of record Preferred Stock immediately prior to an automatic conversion shall be entitled to all declared but unpaid dividends up to the time of the automatic conversion. Such dividends shall be paid to all such holders within thirty (30) days of the automatic conversion.

(c) Mechanics of Conversion.

(i) No fractional shares of Common Stock shall be issued upon conversion of Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall pay cash equal to such fraction multiplied by the then effective applicable Conversion Price. Before any holder of Preferred Stock shall be entitled to convert the same into full shares of Common Stock, such holder shall surrender the certificate or certificates therefor, duly endorsed, at the office of the Corporation or of any transfer agent for the Preferred Stock, and shall give written notice to the Corporation at such office that such holder elects to convert the same and shall state therein his name or the name or names of his nominees in which such holder wishes the certificate or certificates for shares of Common Stock to be issued, together with the applicable federal taxpayer identification number. The Corporation shall, as soon as practicable thereafter, issue and deliver to such holder of Preferred Stock, or to his nominee or nominees, a certificate or certificates for the number of shares of Common Stock to which he shall be entitled, together with cash in lieu of any fraction of a share. Subject to Section 3.3(b) above, such conversion shall be deemed to have been made immediately prior to the close of business on the date of such surrender of the shares of Preferred

Stock to be converted, and the person or persons entitled to receive the shares of Common Stock issuable upon conversion shall be treated for all purposes as the record holder or holders of such shares of Common Stock on such date.

(ii) If the conversion is in connection with an underwritten offering of securities pursuant to the Securities Act, the conversion may, at the option of any holder tendering shares of Preferred Stock for conversion, be conditioned upon the closing with the underwriters of the sale of securities pursuant to such offering, in which event the person(s) entitled to receive the Common Stock upon conversion of the Preferred Stock shall not be deemed to have converted such Preferred Stock until immediately prior to the closing of such sale of securities.

(d) Adjustments to Conversion Prices for Diluting Issues:

(i) Special Definitions. For purposes of this Article Fourth, the following definitions shall apply:

(1) "Option" shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire either Common Stock or Convertible Securities (as defined below).

(2) "Second Series D Original Issue Date" shall mean the date on which the first share of Series D Preferred Stock was issued pursuant to the Second Series D Purchase Agreement.

(3) "Convertible Securities" shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(4) "Additional Shares of Common Stock" shall mean all shares of Common Stock issued (or, pursuant to Section 3.3(d)(iii), deemed to be issued) by the Corporation after the Second Series D Original Issue Date, other than the following shares of Common Stock, and shares of Common Stock deemed issued pursuant to the following Options and Convertible Securities ("Exempted Securities"):

(A) shares of Common Stock issued upon conversion of shares of Preferred Stock or shares of Common Stock issued by way of a dividend or distribution on shares of Preferred Stock;

(B) shares of Common Stock or Options to purchase shares of Common Stock, up to an aggregate of 15,900,000 shares of Common Stock, issued to officers, directors or employees of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to any stock purchase or option plan or other employee or director stock incentive or compensation agreement or program (each, a "Plan") approved by the Board of Directors, including a majority of the Preferred Directors;

(C) shares of Common Stock, Options or Convertible Securities issued in consideration for the acquisition or licensing of technology or a corporate partnership transaction, if approved by the Board of Directors, including a majority of the Preferred Directors not abstaining from voting on the matter;

(D) shares of Common Stock, Options or Convertible Securities issued pursuant to debt financing, equipment leasing or real property leasing transactions, if approved by the Board of Directors, including a majority of the Preferred Directors;

(E) shares of Common Stock issued to the public in connection with a Qualified IPO;

(F) shares of Common Stock, Options or Convertible Securities issued to suppliers or third party service providers in connection with the provision of goods or services pursuant to transactions approved by the Board of Directors, including a majority of the Preferred Directors;

(G) shares of Common Stock, Options or Convertible Securities issued (i) to a target corporation or its stockholders pursuant to the acquisition of such corporation by the Corporation by merger, purchase of substantially all of the assets or other reorganization or (ii) pursuant to a joint venture agreement, provided that such issuances are approved by the Board of Directors, including a majority of the Preferred Directors not abstaining from voting on the matter;

(H) Preferred Stock issued or issuable upon the exercise of that certain Preferred Stock Purchase Warrant issued by the Corporation to Lighthouse Capital Partners VI, L.P. on December 6, 2011, as amended, and Common Stock issued or issuable upon the conversion of such Preferred Stock;

(I) Preferred Stock issued or issuable upon the exercise of that certain Warrant issued by the Corporation to Silicon Valley Bank on August 8, 2008, and Common Stock issued or issuable upon the conversion of such Preferred Stock;

(J) Preferred Stock issued or issuable upon the exercise of those certain Stock Purchase Warrants issued by the Corporation on May 26, 2010 and September 29, 2010, and Common Stock issued or issuable upon the conversion of such Preferred Stock; and

(K) shares of Common Stock or Convertible Securities actually issued upon the exercise of Options or shares of Common Stock actually issued upon the conversion or exchange of Convertible Securities, in each case provided such issuance is pursuant to the terms of such Option or Convertible Security as in effect as of the time of such issue.

(ii) No Adjustment of Conversion Prices.

(1) No adjustment in the Seed Conversion Price shall be made due to the issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Seed Preferred Stock agreeing that no such adjustment shall be made due to such issuance.

(2) No adjustment in the Series A Conversion Price shall be made due to the issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of at least sixty percent (60%) in voting power of the then outstanding Series A Preferred Stock agreeing that no such adjustment shall be made due to such issuance.

(3) No adjustment in the Series B Conversion Price shall be made due to the issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of at least sixty percent (60%) in voting power of the then outstanding Series B Preferred Stock agreeing that no such adjustment shall be made due to such issuance.

(4) No adjustment in the Series B-1 Conversion Price shall be made due to the issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of at least sixty percent (60%) in voting power of the then outstanding Series B-1 Preferred Stock agreeing that no such adjustment shall be made due to such issuance.

(5) No adjustment in the Series C Conversion Price shall be made due to the issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of at least sixty percent (60%) in voting power of the then outstanding Series C Preferred Stock agreeing that no such adjustment shall be made due to such issuance.

(6) No adjustment in the Series D Conversion Price shall be made due to the issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of at least sixty percent (60%) in voting power of the then outstanding Series D Preferred Stock agreeing that no such adjustment shall be made due to such issuance.

(iii) Deemed Issue of Additional Shares of Common Stock.

(1) Options and Convertible Securities. In the event the Corporation at any time or from time to time after the Second Series D Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities that are themselves Exempted Securities) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provisions contained therein for a subsequent adjustment of such number) of Common Stock issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(2) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to any Conversion Price pursuant to the terms of Section 3.3(d)(iv), are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (x) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or

Convertible Security or (y) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the Conversion Prices computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to such Conversion Prices as would have obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this Section 3.3(d)(iii)(2) shall have the effect of increasing the Conversion Price for any series of Preferred Stock to an amount which exceeds the lower of (i) the Conversion Price for such series of Preferred Stock in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or (ii) the Conversion Price for such series of Preferred Stock that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(3) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities which are themselves Exempted Securities), the issuance of which did not result in an adjustment to a Conversion Price pursuant to the terms of Section 3.3(d)(iv) (either because the consideration per share (determined pursuant to Section 3.3(d)(v)) of the Additional Shares of Common Stock subject thereto was equal to or greater than such Conversion Price then in effect, or because such Option or Convertible Security was issued before the Second Series D Original Issue Date), are revised after the Second Series D Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Section 3.3(d)(iii)(1)) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(4) If a record date shall have been fixed for the determination of holders of any class of securities entitled to receive any Options or Convertible Securities (excluding Options or Convertible Securities which are themselves Exempted Securities), and such Options or Convertible Securities are not issued on the date fixed therefor, any adjustment previously made in any Conversion Price which became effective on such record date shall be canceled as of the close of business as of such record date, and thereafter each Conversion Price shall be adjusted pursuant to the terms of this Section 3.3(d)(iii) as of the actual date of issuance of such Options or Convertible Securities.

(5) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) which resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to any Conversion Price pursuant to the terms of Section 3.3(d)(iv), such Conversion Price shall be readjusted to

such Conversion Price as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(6) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to any Conversion Price provided for in this Section 3.3(d)(iii) shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Section 3.3(d)(iii)). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to a Conversion Price that would result under the terms of this Section 3.3(d)(iii) at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to such Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

(7) Stock Dividends, Stock Distributions and Subdivisions. In the event the Corporation at any time or from time to time after the Second Series D Original Issue Date shall declare or pay any dividend or make any other distribution on the Common Stock payable in Common Stock or in any right to acquire Common Stock for no consideration, or effect a subdivision of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in Common Stock), then and in any such event, Additional Shares of Common Stock shall not be deemed to have been issued pursuant to Section 3.3(d)(iv), but the Seed Conversion Price, Series A Conversion Price, Series B Conversion Price, Series B-1 Conversion Price, Series C Conversion Price or Series D Conversion Price, as the case may be, shall be adjusted in accordance with Section 3.3(d)(vi).

(iv) Adjustment of Conversion Price Upon Issuance of Additional Shares of Common Stock.

(1) In the event the Corporation shall at any time after the Second Series D Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 3.3(d)(iii)(1)) without consideration or for a consideration per share less than the Seed Conversion Price in effect on the date of and immediately prior to such issue, then and in such event, such Seed Conversion Price shall be reduced, concurrently with such issue in order to increase the number of shares of Common Stock into which the Seed Preferred Stock is convertible, to a price (calculated to the nearest cent) determined by dividing (A) (i) the Seed Conversion Price in effect immediately prior to such issue multiplied by the number of shares of Common Stock outstanding immediately prior to such issue (including all shares of Common Stock issuable upon exercise or conversion of any outstanding Options, Convertible Securities and shares of the Preferred Stock), plus (ii) the aggregate consideration received by the Corporation for the total number of

Additional Shares of Common Stock so issued, by (B) (i) the number of shares of Common Stock outstanding immediately prior to such issue (including all shares of Common Stock issuable upon exercise or conversion of any outstanding Options, Convertible Securities and shares of Preferred Stock), plus (ii) the total number of such Additional Shares of Common Stock so issued, provided that the Seed Conversion Price shall not be so reduced at such time if the amount of such reduction would be an amount less than $0.01, but any such amount shall be carried forward and any reduction with respect thereto shall be made at the time of and together with any subsequent reduction which, together with such amount and any other amount or amounts so carried forward, shall aggregate $0.01 or more.

(2) In the event the Corporation shall at any time after the Second Series D Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 3.3(d)(iii)(1)) without consideration or for a consideration per share less than the Series A Conversion Price in effect on the date of and immediately prior to such issue, then and in such event, such Series A Conversion Price shall be reduced, concurrently with such issue in order to increase the number of shares of Common Stock into which the Series A Preferred Stock is convertible, to a price (calculated to the nearest cent) determined by dividing (A) (i) the Series A Conversion Price in effect immediately prior to such issue multiplied by the number of shares of Common Stock outstanding immediately prior to such issue (including all shares of Common Stock issuable upon exercise or conversion of any outstanding Options, Convertible Securities and shares of the Preferred Stock), plus (ii) the aggregate consideration received by the Corporation for the total number of Additional Shares of Common Stock so issued, by (B) (i) the number of shares of Common Stock outstanding immediately prior to such issue (including all shares of Common Stock issuable upon exercise or conversion of any outstanding Options, Convertible Securities and shares of Preferred Stock), plus (ii) the total number of such Additional Shares of Common Stock so issued, provided that the Series A Conversion Price shall not be so reduced at such time if the amount of such reduction would be an amount less than $0.01, but any such amount shall be carried forward and any reduction with respect thereto shall be made at the time of and together with any subsequent reduction which, together with such amount and any other amount or amounts so carried forward, shall aggregate $0.01 or more.

(3) In the event the Corporation shall at any time after the Second Series D Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 3.3(d)(iii)(1)) without consideration or for a consideration per share less than the Series B Conversion Price in effect on the date of and immediately prior to such issue, then and in such event, such Series B Conversion Price shall be reduced, concurrently with such issue in order to increase the number of shares of Common Stock into which the Series B Preferred Stock is convertible, to a price (calculated to the nearest cent) determined by dividing (A) (i) the Series B Conversion Price in effect immediately prior to such issue multiplied by the number of shares of Common Stock outstanding immediately prior to such issue (including all shares of Common Stock issuable upon exercise or conversion of any outstanding Options, Convertible Securities and shares of the Preferred Stock), plus (ii) the aggregate consideration received by the Corporation for the total number of Additional Shares of Common Stock so issued, by (B) (i) the number of shares of Common Stock outstanding immediately prior to such issue (including all shares of Common Stock issuable upon exercise or conversion of any outstanding Options, Convertible Securities

and shares of Preferred Stock), plus (ii) the total number of such Additional Shares of Common Stock so issued, provided that the Series B Conversion Price shall not be so reduced at such time if the amount of such reduction would be an amount less than $0.01, but any such amount shall be carried forward and any reduction with respect thereto shall be made at the time of and together with any subsequent reduction which, together with such amount and any other amount or amounts so carried forward, shall aggregate $0.01 or more.

(4) In the event the Corporation shall at any time after the Second Series D Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 3.3(d)(iii)(1)) without consideration or for a consideration per share less than the Series B-1 Conversion Price in effect on the date of and immediately prior to such issue, then and in such event, such Series B-1 Conversion Price shall be reduced, concurrently with such issue in order to increase the number of shares of Common Stock into which the Series B-1 Preferred Stock is convertible, to a price (calculated to the nearest cent) determined by dividing (A)(i) the Series B-1 Conversion Price in effect immediately prior to such issue multiplied by the number of shares of Common Stock outstanding immediately prior to such issue (including all shares of Common Stock issuable upon exercise or conversion of any outstanding Options, Convertible Securities and shares of Preferred Stock), plus (ii) the aggregate consideration received by the Corporation for the total number of Additional Shares of Common Stock so issued, by (B) (i) the number of shares of Common Stock outstanding immediately prior to such issue (including all shares of Common Stock issuable upon exercise or conversion of any outstanding Options, Convertible Securities and shares of Preferred Stock), plus (ii) the total number of such Additional Shares of Common Stock so issued, provided that the Series B-1 Conversion Price shall not be so reduced at such time if the amount of such reduction would be an amount less than $0.01, but any such amount shall be carried forward and any reduction with respect thereto shall be made at the time of and together with any subsequent reduction which, together with such amount and any other amount or amounts so carried forward, shall aggregate $0.01 or more.

(5) In the event the Corporation shall at any time after the Second Series D Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 3.3(d)(iii)(1)) without consideration or for a consideration per share less than the Series C Conversion Price in effect on the date of and immediately prior to such issue, then and in such event, such Series C Conversion Price shall be reduced, concurrently with such issue in order to increase the number of shares of Common Stock into which the Series C Preferred Stock is convertible, to a price (calculated to the nearest cent) determined by dividing (A) (i) the Series C Conversion Price multiplied by the number of shares of Common Stock outstanding immediately prior to such issue (including shares of Common Stock issuable upon conversion of any outstanding Options, Convertible Securities and shares of the Preferred Stock), plus (ii) the aggregate consideration received by the Corporation for the total number of Additional Shares of Common Stock so issued, by (B) (i) the number of shares of Common Stock outstanding immediately prior to such issue (including shares of Common Stock issuable upon conversion of any outstanding Options, Convertible Securities and shares of Preferred Stock), plus (ii) the total number of such Additional Shares of Common Stock so issued, provided that the Series C Conversion Price shall not be so reduced at such time if the amount of such reduction would be an amount less than $0.01, but any such amount shall be carried forward and any reduction with respect thereto shall be made at the time

of and together with any subsequent reduction which, together with such amount and any other amount or amounts so carried forward, shall aggregate $0.01 or more.

(6) In the event the Corporation shall at any time after the Second Series D Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 3.3(d)(iii)(1)) without consideration or for a consideration per share less than the Series D Conversion Price in effect on the date of and immediately prior to such issue, then and in such event, such Series D Conversion Price shall be reduced, concurrently with such issue in order to increase the number of shares of Common Stock into which the Series D Preferred Stock is convertible, to a price (calculated to the nearest cent) determined by dividing (A) (i) the Series D Conversion Price multiplied by the number of shares of Common Stock outstanding immediately prior to such issue (including shares of Common Stock issuable upon conversion of any outstanding Options, Convertible Securities and shares of the Preferred Stock), plus (ii) the aggregate consideration received by the Corporation for the total number of Additional Shares of Common Stock so issued, by (B) (i) the number of shares of Common Stock outstanding immediately prior to such issue (including shares of Common Stock issuable upon conversion of any outstanding Options, Convertible Securities and shares of Preferred Stock), plus (ii) the total number of such Additional Shares of Common Stock so issued, provided that the Series D Conversion Price shall not be so reduced at such time if the amount of such reduction would be an amount less than $0.01, but any such amount shall be carried forward and any reduction with respect thereto shall be made at the time of and together with any subsequent reduction which, together with such amount and any other amount or amounts so carried forward, shall aggregate $0.01 or more.

(7) In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to any Conversion Price pursuant to the terms of this Section 3.3(d), then, upon the final such issuance, such Conversion Price shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

(v) Determination of Consideration. For purposes of this Section 3.3(d), the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(1) Cash and Property. Such consideration shall:

(A) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation excluding amounts paid or payable for accrued interest or accrued dividends;

(B) insofar as it consists of property other than cash, be computed at the fair value thereof at the time of such issue, as determined in good faith by the Board of Directors; and

(C) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration which covers both, be the proportion of such consideration so received, computed as provided in clauses (A) and (B) above, as determined in good faith by the Board of Directors.

(2) Options and Convertible Securities. The aggregate consideration received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Section 3.3(d)(iii)(1), relating to Options and Convertible Securities, shall be determined by computing the total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration until such subsequent adjustment occurs) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities. The total number of Additional Shares of Common Stock so issued shall be determined by calculating the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number until such subsequent adjustment occurs) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities.

(vi) Adjustment for Dividends, Distributions, Subdivisions Combinations or Consolidation of Common Stock.

(1) Adjustment for Certain Dividends and Distributions. In the event the Corporation at any time or from time to time after the Second Series D Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common Stock, then and in each such event the Conversion Price for each series of Preferred Stock in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying such Conversion Price then in effect by a fraction:

(A) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and

(B) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing, (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the Conversion Price for each series of Preferred Stock shall be recomputed accordingly as of the close of business on such record date and thereafter the Conversion Price for such series of Preferred

Stock shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) that no such adjustment shall be made if the holders of the Preferred Stock simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

(2) Adjustment for Stock Splits and Combinations. If the Corporation shall at any time or from time to time after the Second Series D Original Issue Date effect a subdivision of the outstanding Common Stock, the Conversion Price for each series of Preferred Stock in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time after the Second Series D Original Issue Date combine the outstanding shares of Common Stock, the Conversion Price for each series of Preferred Stock in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

(3) Adjustments for Other Dividends and Distributions. In the event the Corporation at any time or from time to time after the Second Series D Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 3.5 do not apply to such dividend or distribution, then and in each such event the holders of Preferred Stock shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

(vii) Adjustment for Merger or Reorganization. Subject to provisions of Section 3.2 above, in case of any reorganization, recapitalization, reclassification, consolidation or merger involving the Corporation in which the Common Stock (but not all shares of the Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by Section 3.3(d)(vi)), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each share of Preferred Stock not so converted or exchanged shall thereafter be convertible into the number of shares of stock or other securities or property to which a holder of the number of shares of Common Stock of the Corporation deliverable upon conversion of such share of Preferred Stock would have been entitled upon such reorganization, recapitalization, reclassification, consolidation or merger. In any such case, appropriate adjustment (as determined in good faith by the Board of Directors) shall be made in the application of these provisions set forth with respect to the rights and interest thereafter of the holders of Seed Preferred Stock, Series A Preferred Stock, Series B

Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock, to the end that these provisions (including provisions with respect to changes in and other adjustments of the applicable Conversion Price) shall thereafter be applicable, as nearly as reasonably may be, in relation to any shares of stock or other property thereafter deliverable upon the conversion of the Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock.

(e) No Impairment. The Corporation will not, by amendment of its Certificate of Incorporation or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed hereunder by the Corporation without the written consent of the holders of at least fifty-eight percent (58%) in voting power of the then outstanding shares of the series of Preferred Stock affected, but will at all times in good faith assist in the carrying out of all the provisions of this Section 3.3 and in the taking of all such action as may be necessary or appropriate in order to protect the Conversion Rights of the holders of Preferred Stock against impairment.

(f) Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of any Conversion Price pursuant to this Section 3.3, the Corporation at its expense shall promptly compute such adjustment or readjustment in accordance with these terms and furnish to each holder of Preferred Stock, as the case may be, a certificate setting forth such adjustment, readjustment or conversion and showing in detail the facts upon which such adjustment, readjustment or conversion is based, provided that the failure to promptly provide such notice shall not affect the effectiveness of such adjustment, or readjustment or conversion. The Corporation shall, upon the written request at any time of any holder of Preferred Stock, furnish or cause to be furnished to such holder a like certificate setting forth (i) such adjustments and readjustments, (ii) the Seed Conversion Price, Series A Conversion Price, Series B Conversion Price, Series B-1 Conversion Price, Series C Conversion Price or Series D Conversion Price, as the case may be, then in effect, and (iii) the number of shares of Common Stock and the amount, if any, of other property which at the time would be received upon the conversion of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock or Series D Preferred Stock, as the case may be.

(g) Notices of Record Date. In the event of (i) any taking by Corporation of a record date of the holders of any class of securities for the purpose of determining the holders thereof who are entitled to receive any dividend or other distribution or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security, or (ii) any capital reorganization of the Corporation, any reclassification or recapitalization of the capital stock of the Corporation or any Liquidating Event, the Corporation shall mail to each holder of Preferred Stock at least ten (10) days prior to the record date or effective date for the event specified therein, a notice specifying (A) the date on which any such record is to be taken for the purpose of such dividend, distribution or right and a description of such dividend, distribution or right, (B) the date on which any such reorganization, reclassification, recapitalization or Liquidating Event is expected to become effective, and (C) the time, if any, that is to be fixed, as to when the holders of record of Common Stock (or other securities) shall be entitled to exchange their shares of Common Stock (or other securities) for securities or other property deliverable upon such reorganization, reclassification, recapitalization or Liquidating Event.

(h) Common Stock Reserved. The Corporation shall reserve and keep available out of its authorized but unissued Common Stock, solely for the purpose of effecting the conversion of the shares of the Preferred Stock, such number of shares of Common Stock as shall from time to time be sufficient to effect conversion of the Preferred Stock. If at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of the Preferred Stock, the Corporation will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purpose, including, without limitation, engaging in best efforts to obtain the requisite stockholder approval of any necessary amendment to its Certificate of Incorporation.

(i) Special Mandatory Conversion.

(i) Trigger Event. In the event that any holder of shares of Preferred Stock does not participate in a Qualified Financing (as defined below) by purchasing in the aggregate such holder’s Pro Rata Amount (as defined below) of the Qualified Financing within the time period specified by the Corporation (provided that the Corporation has sent to each holder of Preferred Stock at least fifteen (15) business days written notice of, and the opportunity to purchase its Pro Rata Amount of, the Qualified Financing), then the Applicable Portion (as defined below) of the shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and/or Series D Preferred Stock held by such holder shall automatically, and without any further action on the part of such holder, be converted into shares of Common Stock at the Seed Conversion Price, Series A Conversion Price, Series B Conversion Price, Series B-1 Conversion Price, Series C Conversion Price or Series D Conversion Price, as the case may be, in effect immediately prior to the consummation of such Qualified Financing, effective upon, subject to, and concurrently with, the consummation of the Qualified Financing. For purposes of determining the number of shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock owned by a holder, and for determining the number of Offered Securities (as defined below) a holder of Preferred Stock has purchased in a Qualified Financing, all shares of Preferred Stock held by Affiliates (as defined below) of such holder shall be aggregated with such holder’s shares and all Offered Securities purchased by Affiliates of such holder shall be aggregated with the Offered Securities purchased by such holder (provided that no shares or securities shall be attributed to more than one entity or person within any such group of affiliated entities or persons). Such conversion is referred to as a “Special Mandatory Conversion.”

(ii) Procedural Requirements. Upon a Special Mandatory Conversion, each holder of shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock converted pursuant to Section 3.3(i) shall be sent written notice of such Special Mandatory Conversion and the place designated for mandatory conversion of all such shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock or Series D Preferred Stock pursuant to this Section 3.3. Upon receipt of such notice, each holder of such shares of Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Preferred Stock converted pursuant to Section 3.3(i)(i), including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the time of the Special Mandatory Conversion (notwithstanding the failure of the holder or holders thereof to surrender the certificates for such shares at or prior to such time), except only the rights of the holders thereof, upon surrender of their certificate or certificates therefor (or lost certificate affidavit and agreement), to receive the items provided for in the next sentence of this Section 3.3(i)(ii). As soon as practicable after the Special Mandatory Conversion and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Preferred Stock so converted, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Section 3.3(c) in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends on the shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock converted and a new certificate for the number of shares, if any, of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock represented by such surrendered certificate and not converted pursuant to Section 3.3(i)(i). Such converted Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock accordingly.

(iii) Definitions. For purposes of this Section 3.3(i), the following definitions shall apply:

(1) "Affiliate" shall mean, with respect to any holder of shares of Preferred Stock, any person, entity or firm which, directly or indirectly, controls, is controlled by or is under common control with such holder, including, without limitation, any entity of which the holder is a partner or member, any partner, officer, director, member or employee of such holder and any venture capital fund now or hereafter existing of which the holder is a partner or member which is controlled by or under common control with one or more general partners of such holder or shares the same management company with such holder.

(2) “Applicable Portion” shall mean, with respect to any holder of shares of Preferred Stock, a number of shares of Preferred Stock calculated by multiplying the aggregate number of shares of Preferred Stock held by such holder immediately prior to a Qualified Financing by a fraction, the numerator of which is equal to the amount, if positive, by which such holder’s Pro Rata Amount exceeds the number of Offered Securities actually purchased by such holder in such Qualified Financing, and the denominator of which is equal to such holder’s Pro Rata Amount.

(3) “Offered Securities” shall mean the equity securities of the Corporation set aside by the Board of Directors of the Corporation for purchase by holders of outstanding shares of Preferred Stock in connection with a Qualified Financing, and offered to such holders.

(4) “Pro Rata Amount” shall mean, with respect to any holder of Preferred Stock, the lesser of (a) a number of Offered Securities calculated by multiplying the aggregate number of Offered Securities by a fraction, the numerator of which is equal to the number of shares of Common Stock issuable upon conversion of all shares of Preferred Stock then owned by such holder, and the denominator of which is equal to the aggregate number of outstanding shares of Common Stock (for the purpose of this definition, treating all shares of Common Stock issuable upon exercise of Options outstanding immediately prior to such Qualified Financing or upon conversion of Convertible Securities outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such Qualified Financing as outstanding), or (b) the maximum number of Offered Securities that such holder is permitted by the Corporation to purchase in such Qualified Financing, after giving effect to any cutbacks or limitations established by the Board of Directors and applied on a pro rata basis to all holders of Preferred Stock.

(5) “Qualified Financing” shall mean any transaction involving the issuance or sale of Additional Shares of Common Stock on or after the Second Series D Original Issue Date that is determined by the Board of Directors to be a “Qualified Financing.”

(j) Effect of Conversion. All shares of Preferred Stock which shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the effective time of such conversion, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor, to receive payment in lieu of any fraction of a share otherwise issuable upon such conversion as provided in Section 3.3(c)(i) and to receive payment of any dividends declared but unpaid thereon. Any shares of Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series of Preferred Stock, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of such series of Preferred Stock accordingly.

(k) Taxes. The Corporation shall pay any and all issue and other similar taxes that may be payable in respect of any issuance or delivery of shares of Common Stock upon conversion of shares of Preferred Stock. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of shares of Common Stock in a name other than that in which the shares of Preferred Stock so converted were registered, and no such issuance or delivery shall be made unless and until the person or entity requesting such issuance has paid to the Corporation the amount of any such tax or has established, to the satisfaction of the Corporation, that such tax has been paid.

3.4. Voting Rights.

(a) The holders of shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock shall be entitled to notice of any stockholders' meeting and to vote upon any matter submitted to a stockholder for a vote (whether at a meeting or by written consent in lieu of meeting), as though the Common Stock, Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock constituted a single class of stock, except with respect to those matters on which the Delaware General Corporation Law requires that a vote must be by a separate class or classes or by separate series, as to which each such class or series shall have the right to vote in accordance with such law, and except as provided in Sections 2.1 and 3.4(b) and (c), on the following basis: holders of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock shall have that number of votes per share as is equal to the number of shares of Common Stock into which each such share of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock, as the case may be, held by such holder is then convertible.

(b) Any provision of the by-laws of the Corporation to the contrary notwithstanding, the number of directors constituting the entire Board of Directors of the Corporation shall initially be fixed at seven (7) and may not be increased or decreased without the prior written consent of a majority of the Preferred Directors (as defined in Section 3.4(c) below).

(c) The Board of Directors shall not delegate any of its powers or duties to any committee of the Board of Directors without the consent of a majority of the Preferred Directors, and any committee of the Board of Directors shall include the Series C Director (as defined below), except in the case of an ad-hoc or special committee where service of the Series C Director on such committee would, in the good faith judgment of the Board of Directors, present a conflict of interest on the part of the Series C Director.

(d) At all times during which shares of Seed Preferred Stock remain outstanding, the holders of the outstanding shares of Seed Preferred Stock shall have the exclusive right, separately from the Common Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock, to elect one director of the Corporation (the "Seed Director"). The Seed Director shall be elected by the vote or written consent of the holders of a majority in voting power of the outstanding Seed Preferred Stock voting as a separate class. At all times during which shares of Series A Preferred Stock remain outstanding, the holders of the outstanding shares of Series A Preferred Stock shall have the exclusive right, separately from the Common Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series

D Preferred Stock, to elect one director of the Corporation (the “Series A Director”), which director shall be elected by the vote or written consent of the holders of at least sixty percent (60%) in voting power of the outstanding Series A Preferred Stock voting as a separate class. At all times during which shares of Series C Preferred Stock remain outstanding, the holders of the outstanding shares of Series C Preferred Stock shall have the exclusive right, separately from the Common Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock and Series D Preferred Stock, to elect one director of the Corporation (the “Series C Director”), which director shall be elected by the vote or written consent of the holders of at least sixty percent (60%) in voting power of the outstanding Series C Preferred Stock voting as a separate class. At all times during which shares of Series D Preferred Stock remain outstanding, the holders of the outstanding shares of Series D Preferred Stock shall have the exclusive right, separately from the Common Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock and Series C Preferred Stock, to elect one director of the Corporation (the “Series D Director” and, together with the Seed Director, the Series A Director and the Series C Director, the “Preferred Directors”), which director shall be elected by the vote or written consent of the holders of at least sixty percent (60%) in voting power of the outstanding Series D Preferred Stock voting as a separate class. If any Preferred Director shall cease to serve as a director for any reason, then a director to hold office for the unexpired term of such directorship may be elected by the holders of the Seed Preferred Stock in the case of the Seed Director, by the holders of the Series A Preferred Stock in the case of the Series A Director, by the holders of the Series C Preferred Stock in the case of the Series C Director and by the holders of the Series D Preferred Stock in the case of the Series D Director. A Preferred Director may be removed, with or without cause, and a replacement Preferred Director may be elected in his or her stead, at any time by the affirmative vote at a meeting of stockholders called for the purpose, or by written consent, of the holders of a majority of the then-outstanding shares of Seed Preferred Stock in the case of the Seed Director, by the holders of at least sixty percent (60%) in voting power of the then outstanding shares of Series A Preferred Stock in the case of the Series A Director, by the holders of at least sixty percent (60%) in voting power of the then outstanding shares of Series C Preferred Stock in the case of the Series C Director and by the holders of at least sixty percent (60%) in voting power of the then outstanding shares of Series D Preferred Stock in the case of the Series D Director.

3.5. Dividend Right.

(a) The holders of outstanding Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock shall be entitled to receive, out of funds legally available therefor, prior and in preference to any dividend paid on the Seed Preferred Stock or the Common Stock, cash dividends at the rate of (i) in the case of the Series A Preferred Stock, eight percent (8%) of the Series A Original Issue Price per annum on each outstanding share of Series A Preferred Stock, (ii) in the case of the Series B Preferred Stock, eight percent (8%) of the Series B Original Issue Price per annum on each outstanding share of Series B Preferred Stock, (iii) in the case of the Series B-1 Preferred Stock, eight percent (8%) of the Series B-1 Original Issue Price per annum on each outstanding share of Series B-1 Preferred Stock, (iv) in the case of the Series C Preferred Stock, eight percent (8%) of the Series C Original Issue Price per annum on each outstanding share of Series C Preferred Stock and (v) in the case of the Series D Preferred Stock, eight percent (8%) of the Series D Original Issue Price per annum on each outstanding share of Series D Preferred Stock.

Such dividends shall be payable when, as and if declared by the Board of Directors and before any dividend is declared, paid or set aside on any shares of Common Stock or Seed Preferred Stock.

(b) The holders of outstanding Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock shall be entitled to receive a dividend (determined on the basis of the number of shares of Common Stock into which a share of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock, as the case may be is then convertible) equal to any dividend paid on Common Stock (other than dividends payable solely in shares of Common Stock). Such dividends on Common Stock, if any, shall be payable when, as and if declared by the Board of Directors and before any dividend is declared, paid or set aside on any shares of Common Stock or Seed Preferred Stock.

(c) Any declared and unpaid dividend shall be payable on liquidation, conversion or redemption in accordance with Sections 3.2, 3.3 or 3.7.

(d) In the event the Corporation shall declare a distribution on the Common Stock payable in securities of other persons, evidences of indebtedness issued by the Corporation or other persons, assets (excluding cash dividends) or options or rights to purchase any such securities or evidences of indebtedness, then, in each such case the holders of the Preferred Stock shall be entitled to a proportionate share of any such distribution as though the holders of the Preferred Stock were the holders of the number of shares of Common Stock of the Corporation into which their respective shares of Preferred Stock are convertible as of the record date fixed for the determination of the holders of Common Stock of the Corporation entitled to receive such distribution.

3.6. Covenants. In addition to Section 3.4 and any vote which the Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and/or Series D Preferred Stock may have under Delaware law, so long as at least ten percent (10%) of the shares of Preferred Stock outstanding as of the Second Series D Original Issue Date shall be outstanding, the Corporation shall not (whether by amendment, merger, or otherwise), without first obtaining the affirmative vote or written consent of at least fifty-eight percent (58%) in voting power of all then-outstanding shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock, voting together as a single class:

(a) amend or repeal any provision of, or add any provision to, the Corporation’s Certificate of Incorporation or by-laws;

(b) authorize or effect a change of control, Liquidating Event or other merger or consolidation, reincorporation, recapitalization, consolidation, share exchange, reorganization or other similar transaction involving the Corporation;

(c) authorize or effect any sale, lease, license or other transfer or disposition of all or substantially all of the Corporation’s assets;

(d) create or authorize the creation of, or issue or obligate itself to issue shares of, or reclassify any shares of capital stock into, any class or series of stock having rights of redemption, liquidation preference, voting or dividend rights on parity with or having preference over any series of the Preferred Stock or any Options or Convertible Securities exercisable for or convertible into shares of any such class or series of stock;

(e) effect any acquisition of (i) the capital stock of another entity which results in the consolidation of that entity into the results of operations of the Corporation or (ii) all or substantially all of the assets of another entity;

(f) incur any indebtedness for borrowed money in an amount in excess of $500,000;

(g) create or adopt a new plan for the grant of stock options or the issuance of restricted stock to employees, consultants, directors, or officers of the Corporation or increase the number of shares available under any such existing plan;

(h) pay or declare any dividend or distribution on any shares of the Corporation’s capital stock (except dividends payable solely in shares of Common Stock), or apply any of the Corporation’s assets to the redemption or repurchase of the Corporation’s capital stock (except for acquisitions of Common Stock by the Corporation from former employees, consultants or other service providers pursuant to agreements in a form approved by the Board of Directors which permit the Corporation to repurchase such shares at cost (or the lesser of cost or fair market value) upon termination of services to the Corporation or acquisitions of Common Stock in exercise of the Corporation’s right of first refusal to repurchase such shares;

(i) increase or decrease the authorized number of directors of the Corporation, except as permitted by Section 3.4(b) hereof;

(j) enter into, agree to enter into or execute any transaction with any officer, director or affiliate of the Corporation (as such term is defined in the regulations promulgated under the Securities Act) unless approved by a disinterested majority of the Board of Directors;

(k) authorize or effect any change in the fundamental business of the Corporation, which is currently the discovery and development of human therapeutics;

(l) authorize or undertake any public offering of any securities of the Corporation other than in a Qualified IPO;

(m) allow any family member, or spouse thereof, of a stockholder or an officer of the Corporation to be employed by the Corporation as an employee, consultant, advisor or other service provider without prior approval of the Audit Committee of the Board of Directors; or

(n) permit any wholly-owned subsidiary to undertake any of the actions described in Sections 3.6(a) through 3.6(m) unless approved by the Board of Directors, including a majority of the Preferred Directors not abstaining from voting on the matter.

3.7. Redemption.

(a) Redemption. Shares of Preferred Stock shall be redeemed by the Corporation out of funds lawfully available therefor at a price per share equal to the Seed Original Issue Price, the Series A Original Issue Price, the Series B Original Issue Price, the Series B-1 Original Issue Price, the Series C Original Issue Price or the Series D Original Issue Price, as applicable, plus all declared but unpaid dividends thereon (the "Redemption Price"), in three annual installments commencing not more than 30 days after receipt by the Corporation at any time on or after the fifth anniversary of the Second Series D Original Issue Date, from the holders of at least fifty-eight percent (58%) in voting power of the then-outstanding shares of Preferred Stock, of written notice requesting redemption of all shares of Preferred Stock. The date of each such installment shall be referred to as a "Redemption Date". On each Redemption Date, the Corporation shall redeem, on a pro rata basis in accordance with the number of shares of Preferred Stock owned by each holder, that number of outstanding shares of Preferred Stock determined by dividing (i) the total number of shares of Preferred Stock outstanding immediately prior to such Redemption Date by (ii) the number of remaining Redemption Dates (including the Redemption Date to which such calculation applies); provided, however, that Excluded Shares (as defined below) shall not be redeemed and shall be excluded from the calculations set forth in this sentence. If the Corporation does not have sufficient funds legally available to redeem on any Redemption Date all shares of Preferred Stock to be redeemed on such Redemption Date, the Corporation shall redeem a pro rata portion of each holder's redeemable shares of such capital stock out of funds legally available therefor, based on the respective amounts which would otherwise be payable in respect of the shares to be redeemed if the legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares to have been redeemed as soon as practicable after the Corporation has funds legally available therefor.

(b) Redemption Notice. The Corporation shall send written notice of the mandatory redemption (the "Redemption Notice") to each holder of record of Preferred Stock not less than 10 days prior to each Redemption Date. Each Redemption Notice shall state:

(i) the number of shares of Preferred Stock held by the holder that the Corporation shall redeem on the Redemption Date specified in the Redemption Notice;

(ii) the Redemption Date and the Redemption Price;

(iii) the then-applicable rate at which the shares of Preferred Stock held by each holder may be converted into Common Stock prior to such Redemption Date; and

(iv) that the holder is to surrender to the Corporation, in the manner and at the place designated, his, her or its certificate or certificates representing the shares of Preferred Stock to be redeemed.

If the Corporation receives, on or prior to the 5th day after the date of delivery of the Redemption Notice to a holder of Preferred Stock, written notice from such holder that such holder elects to be excluded from the redemption provided in this Section 3.7, then the shares of Preferred Stock registered on the books of the Corporation in the name of such holder at the time of the Corporation's receipt of such notice shall thereafter be "Excluded Shares". Excluded

Shares shall not be redeemed or redeemable pursuant to this Section 3.7, whether on such Redemption Date or thereafter.

(c) Surrender of Certificates; Payment. On or before the applicable Redemption Date, each holder of shares of Preferred Stock to be redeemed on such Redemption Date, unless such holder has exercised his, her or its right to convert such shares as provided in Section 3.3, shall surrender the certificate or certificates representing such shares (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation, in the manner and at the place designated in the Redemption Notice, and thereupon the Redemption Price for such shares shall be payable to the order of the person whose name appears on such certificate or certificates as the owner thereof. In the event less than all of the shares of Preferred Stock represented by a certificate are redeemed, a new certificate representing the unredeemed shares of Preferred Stock shall promptly be issued to such holder.

(d) Rights Subsequent to Redemption. If the Redemption Notice shall have been duly given, and if on the applicable Redemption Date the Redemption Price payable upon redemption of the shares of Preferred Stock to be redeemed on such Redemption Date is paid or tendered for payment or deposited with an independent payment agent so as to be available therefor in a timely manner, then notwithstanding that the certificates evidencing any of the shares of Preferred Stock so called for redemption shall not have been surrendered, dividends with respect to such shares of Preferred Stock shall cease to accrue after such Redemption Date and all rights with respect to such shares shall forthwith after the Redemption Date terminate, except only the right of the holders to receive the Redemption Price without interest upon surrender of their certificate or certificates therefor.

3.8. Converted, Redeemed or Otherwise Acquired Shares. Any share of Preferred Stock that is converted under Section 3.3, or redeemed or otherwise acquired by the Corporation, will be canceled and will not be reissued, sold or transferred.

3.9. Residual Rights. All rights accruing to the outstanding shares of the Corporation not expressly provided for to the contrary shall be vested in the Common Stock.

3.10. Waiver. Any of the rights of the holders of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock set forth herein may be waived by the affirmative consent or vote of the holders of shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock representing at least fifty-eight percent (58%) in voting power of the shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock then outstanding, considered as a single class on an as-converted basis, provided such waiver by its terms is equally applicable to the holders of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock. Any of the rights of the holders of Seed Preferred Stock set forth herein may be waived (in a manner that does not apply to the holders of

Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock or Series D Preferred Stock) by the affirmative consent or vote of the holders of at least a majority of the shares of Seed Preferred Stock then outstanding. Any of the rights of the holders of Series A Preferred Stock set forth herein may be waived (in a manner that does not apply to the holders of Seed Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock or Series D Preferred Stock) by the affirmative consent or vote of the holders of at least sixty percent (60%) of the shares of Series A Preferred Stock then outstanding. Any of the rights of the holders of Series B Preferred Stock set forth herein may be waived (in a manner that does not apply to the holders of Seed Preferred Stock, Series A Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock or Series D Preferred Stock) by the affirmative consent or vote of the holders of at least sixty percent (60%) of the shares of Series B Preferred Stock. Any of the rights of the holders of Series B-1 Preferred Stock set forth herein may be waived (in a manner that does not apply to the holders of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series C Preferred Stock or Series D Preferred Stock) by the affirmative consent or vote of the holders of at least sixty percent (60%) of the shares of Series B-1 Preferred Stock. Any of the rights of the holders of Series C Preferred Stock set forth herein may be waived (in a manner that does not apply to the holders of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock or Series D Preferred Stock) by the affirmative consent or vote of the holders of at least sixty percent (60%) in voting power of the shares of Series C Preferred Stock. Any of the rights of the holders of Series D Preferred Stock set forth herein may be waived (in a manner that does not apply to the holders of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock or Series C Preferred Stock) by the affirmative consent or vote of the holders of at least sixty percent (60%) in voting power of the shares of Series D Preferred Stock.

FIFTH: The election of directors need not be by written ballot unless the by-laws of the Corporation shall so require.

SIXTH: In furtherance and not in limitation of the power conferred upon the Board of Directors by law, the Board of Directors shall have power to make, adopt, alter, amend and repeal from time to time by-laws of the Corporation, subject to the right of the stockholders entitled to vote with respect thereto to alter and repeal by-laws made by the Board of Directors.

SEVENTH: A director of the Corporation shall not be liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except to the extent that exculpation from liability is not permitted under the General Corporation Law as in effect at the time such liability is determined. If the General Corporation Law or any other law of the State of Delaware is amended after approval by the stockholders of this Article SEVENTH to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law as so amended. No amendment or repeal of this Article SEVENTH shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal.

EIGHTH: The Corporation shall, to the maximum extent permitted from time to time under the General Corporation Law, indemnify and upon request advance expenses to any person who is or was a party or is threatened to be made a party to any threatened, pending or completed action, suit, proceeding or claim, whether civil, criminal, administrative or investigative, by reason of the fact that such person is or was or has agreed to be a director or officer of the Corporation or while a director or officer is or was serving at the request of the Corporation as a director, officer, partner, trustee, employee or agent of any corporation, partnership, joint venture, trust or other enterprise, including service with respect to employee benefit plans, against expenses (including attorney's fees and expenses), judgments, fines, penalties and amounts paid in settlement incurred (and not otherwise recovered) in connection with the investigation, preparation to defend or defense of such action, suit, proceeding or claim; provided, however, that the foregoing shall not require the Corporation to indemnify or advance expenses to any person in connection with any action, suit, proceeding, claim or counterclaim initiated by or on behalf of such person. Such indemnification shall not be exclusive of other indemnification rights arising under any by-law, agreement, vote of directors or stockholders or otherwise and shall inure to the benefit of the heirs and legal representatives of such person. Any person seeking indemnification under this Article EIGHTH shall be deemed to have met the standard of conduct required for such indemnification unless the contrary shall be established. Any repeal or modification of the foregoing provisions of this Article EIGHTH shall not adversely affect any right or protection of a director or officer of the Corporation with respect to any acts or omissions of such director or officer occurring prior to such repeal or modification.

NINTH: The Corporation renounces any interest or expectancy of the Corporation in, or in being offered an opportunity to participate in, any Excluded Opportunity. An "Excluded Opportunity" is any matter, transaction or interest that is presented to, or acquired, created or developed by, or which otherwise comes into the possession of, (i) any director of the Corporation who is not an employee of the Corporation or any of its subsidiaries, or (ii) any holder of Preferred Stock or any partner, member, director, stockholder, employee or agent of any such holder, other than someone who is an employee of the Corporation or any of its subsidiaries (collectively, "Covered Persons"), unless such matter, transaction or interest is presented to, or acquired, created or developed by, or otherwise comes into the possession of, a Covered Person expressly and solely in such Covered Person's capacity as a director of the Corporation.

TENTH: The books of the Corporation may (subject to any statutory requirements) be kept outside the State of Delaware as may be designated by the Board of Directors or in the by-laws of the Corporation.

ELEVENTH: If at any time the Corporation shall have a class of stock registered pursuant to the provisions of the Securities Exchange Act of 1934, for so long as such class is so registered, any action by the stockholders of such class must be taken at an annual or special meeting of stockholders and may not be taken by written consent.

3. That the foregoing amendment and restatement was approved by the holders of the requisite number of shares of the Corporation in accordance with Section 228 of the General Corporation Law.

4. That this Amended and Restated Certificate of Incorporation, which restates and integrates and further amends the provisions of the Corporation’s Certificate of Incorporation, as amended, has been duly adopted in accordance with Sections 242 and 245 of the General Corporation Law.

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IN WITNESS WHEREOF, this Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of the Corporation on the 29th day of November, 2012.

By: /s/ Jean Silveri
Jean Silveri
Senior Vice President, General Counsel and Secretary

CERTIFICATE OF AMENDMENT
OF
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Cerulean Pharma Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the “Corporation”), DOES HEREBY CERTIFY AS FOLLOWS:

The Board of Directors of the Corporation duly adopted by written consent, pursuant to Sections 141(f) and 242 of the General Corporation Law of the State of Delaware, a resolution setting forth an amendment to the Certificate of Incorporation of the Corporation and declaring said amendment advisable. The stockholders of the Corporation duly approved said proposed amendment by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolution setting forth the amendment is as follows:

RESOLVED: That Article FOURTH Section 3.3(d)(i)(4)(B) of the Certificate of Incorporation, as amended, of the Corporation be and hereby is deleted in its entirety and the following Article FOURTH Section 3.3(d)(i)(4)(B) is inserted in lieu thereof:

(B) shares of Common Stock or Options to purchase shares of Common Stock, up to an aggregate of 16,900,000 shares of Common Stock, issued to officers, directors or employees of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to any stock purchase or option plan or other employee or director stock incentive or compensation agreement or program (each, a “Plan”) approved by the Board of Directors, including a majority of the Preferred Directors;

IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on the 11th day of January, 2013.

CERULEAN PHARMA INC.

By: /s/ Jean Silveri
Jean Silveri
Senior Vice President, General Counsel
and Secretary

CERTIFICATE OF AMENDMENT
OF
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Cerulean Pharma Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "Corporation"), DOES HEREBY CERTIFY AS FOLLOWS:

The Board of Directors of the Corporation duly adopted by written consent, pursuant to Sections 141(f) and 242 of the General Corporation Law of the State of Delaware, a resolution setting forth an amendment to the Certificate of Incorporation of the Corporation and declaring said amendment advisable. The stockholders of the Corporation duly approved said proposed amendment by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolution setting forth the amendment is as follows:

RESOLVED: That Article FOURTH Section 3.3(d)(i)(4)(B) of the Certificate of Incorporation, as amended, of the Corporation be and hereby is deleted in its entirety and the following Article FOURTH Section 3.3(d)(i)(4)(B) is inserted in lieu thereof:

(B) shares of Common Stock or Options to purchase shares of Common Stock, up to an aggregate of 18,200,000 shares of Common Stock, issued to officers, directors or employees of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to any stock purchase or option plan or other employee or director stock incentive or compensation agreement or program (each, a "Plan") approved by the Board of Directors, including a majority of the Preferred Directors;

IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on the 19th day of February, 2013.

CERULEAN PHARMA INC.

By: /s/ Jean Silveri
Jean Silveri
Senior Vice President, General Counsel
and Secretary

CERTIFICATE OF AMENDMENT
OF
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Cerulean Pharma Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the “Corporation”), DOES HEREBY CERTIFY AS FOLLOWS:

The Board of Directors of the Corporation duly adopted resolutions by written consent in accordance with Section 141(f) of the General Corporation Law of the State of Delaware, setting forth an amendment to the Certificate of Incorporation of the Corporation and declaring said amendment advisable. The stockholders of the Corporation duly approved said proposed amendment by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolution setting forth the amendment is as follows:

RESOLVED: That Article FOURTH, Section 3.4(b) of the Certificate of Incorporation of the Corporation, as amended, be and hereby is deleted in its entirety and the following Article FOURTH, Section 3.4(b) is inserted in lieu thereof:

(b) Any provision of the by-laws of the Corporation to the contrary notwithstanding, the number of directors constituting the entire Board of Directors of the Corporation shall initially be fixed at eight (8) and may not be increased or decreased without the prior written consent of a majority of the Preferred Directors (as defined in Section 3.4(d) below).

RESOLVED: That Article FOURTH, Section 3.4(d) of the Certificate of Incorporation of the Corporation, as amended, be and hereby is deleted in its entirety and the following Article FOURTH, Section 3.4(d) is inserted in lieu thereof:

(d) At all times during which shares of Seed Preferred Stock remain outstanding, the holders of the outstanding shares of Seed Preferred Stock shall have the exclusive right, separately from the Common Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock, to elect one director of the Corporation (the “Seed Director”). The Seed Director shall be elected by the vote or written consent of the holders of a majority in voting power of the outstanding Seed Preferred Stock voting as a separate class. At all times during which shares of Series A Preferred Stock remain outstanding, the holders of the outstanding shares of Series A Preferred Stock shall have the exclusive right, separately from the Common Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock, to elect one director of the Corporation (the “Series A Director”), which director shall be elected by the vote or written consent of the holders of at least sixty percent (60%) in voting power of the outstanding Series A Preferred Stock voting as a separate class. At all times during which shares of Series C Preferred Stock remain outstanding, the holders of the outstanding shares of Series C Preferred Stock shall have the exclusive right, separately from the Common

Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock and Series D Preferred Stock, to elect one director of the Corporation (the “Series C Director”), which director shall be elected by the vote or written consent of the holders of at least sixty percent (60%) in voting power of the outstanding Series C Preferred Stock voting as a separate class. At all times during which shares of Series D Preferred Stock remain outstanding, the holders of the outstanding shares of Series D Preferred Stock shall have the exclusive right, separately from the Common Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock and Series C Preferred Stock, to elect two directors of the Corporation (the “Series D Directors” and, together with the Seed Director, the Series A Director and the Series C Director, the “Preferred Directors”), which directors shall each be elected by the vote or written consent of the holders of at least sixty percent (60%) in voting power of the outstanding Series D Preferred Stock voting as a separate class. If any Preferred Director shall cease to serve as a director for any reason, then a director to hold office for the unexpired term of such directorship may be elected by the holders of the Seed Preferred Stock in the case of the Seed Director, by the holders of the Series A Preferred Stock in the case of the Series A Director, by the holders of the Series C Preferred Stock in the case of the Series C Director and by the holders of the Series D Preferred Stock in the case of the Series D Directors. A Preferred Director may be removed, with or without cause, and a replacement Preferred Director may be elected in his or her stead, at any time by the affirmative vote at a meeting of stockholders called for the purpose, or by written consent, of the holders of a majority of the then-outstanding shares of Seed Preferred Stock in the case of the Seed Director, by the holders of at least sixty percent (60%) in voting power of the then outstanding shares of Series A Preferred Stock in the case of the Series A Director, by the holders of at least sixty percent (60%) in voting power of the then outstanding shares of Series C Preferred Stock in the case of the Series C Director and by the holders of at least sixty percent (60%) in voting power of the then outstanding shares of Series D Preferred Stock in the case of the Series D Directors.

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IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on the 14th day of August, 2013.

CERULEAN PHARMA INC.

By: /s/ Jean Silveri
Jean Silveri
Senior Vice President, General Counsel and Secretary

CERTIFICATE OF AMENDMENT
OF
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Cerulean Pharma Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the “Corporation”), DOES HEREBY CERTIFY AS FOLLOWS:

The Board of Directors of the Corporation duly adopted, pursuant to Sections 141 and 242 of the General Corporation Law of the State of Delaware, resolutions setting forth amendments to the Certificate of Incorporation of the Corporation and declaring said amendments advisable. The stockholders of the Corporation duly approved said proposed amendments by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolutions setting forth the amendments are as follows:

RESOLVED: That Article FOURTH, Section 3.4(b) of the Certificate of Incorporation of the Corporation, as amended, be and hereby is deleted in its entirety and the following Article FOURTH, Section 3.4(b) is inserted in lieu thereof:

(b) Any provision of the by-laws of the Corporation to the contrary notwithstanding, the number of directors constituting the entire Board of Directors of the Corporation shall initially be fixed at ten (10) and may not be increased or decreased without the prior written consent of a majority of the Preferred Directors (as defined in Section 3.4(d) below).

RESOLVED: That Article FOURTH, Section 3.3(d)(i)(4)(B) of the Certificate of Incorporation, as amended, of the Corporation be and hereby is deleted in its entirety and the following Article FOURTH, Section 3.3(d)(i)(4)(B) is inserted in lieu thereof:

(B) shares of Common Stock or Options to purchase shares of Common Stock, up to an aggregate of 18,500,000 shares of Common Stock, issued to officers, directors or employees of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to any stock purchase or option plan or other employee or director stock incentive or compensation agreement or program (each, a “Plan”) approved by the Board of Directors, including a majority of the Preferred Directors;

RESOLVED: That a new clause (vii) is added to Article FOURTH, Section 3.3(a) of the Certificate of Incorporation of the Corporation, as amended, which clause (vii) reads as follows:

(vii) Notwithstanding anything to the contrary contained herein, the holders of Preferred Stock shall not be entitled pursuant to this Section 3.3(a) to convert shares of Preferred Stock into shares of Common Stock commencing at the time of effectiveness of the filing of this Certificate of Amendment of Certificate of Incorporation and ending at 5:00 p.m., Boston, Massachusetts time on the date that is six months after the date of such effectiveness (the “Non-Conversion Period”), provided, however, that such Non-Conversion Period may be shortened or extended with the written consent of holders in interest of at least fifty-eight percent (58%) in voting power of the Preferred Stock outstanding at that time.

IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on the 30 day of January, 2014.

CERULEAN PHARMA INC.

By: /s/ Oliver S. Fetzer
Oliver S. Fetzer
President and Chief Executive Officer

CERTIFICATE OF AMENDMENT
OF
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Cerulean Pharma Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "Corporation"), DOES HEREBY CERTIFY AS FOLLOWS:

The Board of Directors of the Corporation duly adopted, pursuant to Sections 141 and 242 of the General Corporation Law of the State of Delaware, resolutions setting forth an amendment to the Certificate of Incorporation of the Corporation and declaring said amendment advisable. The stockholders of the Corporation duly approved said proposed amendment by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolution setting forth the amendment is as follows:

RESOLVED: That Article FOURTH, Section 3.3(i) of the Certificate of Incorporation of the Corporation, as amended, be and hereby is deleted in its entirety and the following Article FOURTH, Section 3.3(i) is inserted in lieu thereof:

(i) Special Mandatory Conversion.

(i) Trigger Event. In the event that any holder of shares of Preferred Stock does not participate in a Qualified Financing (as defined below) by purchasing in the aggregate such holder's Pro Rata Amount (as defined below) of the Qualified Financing within the time period specified by the Corporation (provided that the Corporation has sent to each holder of Preferred Stock written notice of, and the opportunity to purchase, within fifteen (15) days of such notice, its Pro Rata Amount of, the Qualified Financing), then all shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and/or Series D Preferred Stock held by such holder shall automatically, and without any further action on the part of such holder, be converted into shares of Common Stock at a conversion rate of one (1) share of Common Stock for each ten (10) shares of such series of Preferred Stock, effective upon, subject to, and concurrently with, the consummation of the Qualified Financing, provided, however, if such Qualified Financing is consummated prior to the end of the fifteen (15) day notice period provided for above, such conversion shall occur immediately following such fifteen (15) day period. For purposes of determining the number of shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock owned by a holder, and for determining the number of Offered Securities (as defined below) a holder of Preferred Stock has purchased in a Qualified Financing, all shares of Preferred Stock held by

Affiliates (as defined below) of such holder shall be aggregated with such holder's shares and all Offered Securities purchased by Affiliates of such holder shall be aggregated with the Offered Securities purchased by such holder (provided that no shares or securities shall be attributed to more than one entity or person within any such group of affiliated entities or persons). Such conversion is referred to as a "Special Mandatory Conversion."

(ii) Procedural Requirements. Upon a Special Mandatory Conversion, each holder of shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock converted pursuant to Section 3.3(i) shall be sent written notice of such Special Mandatory Conversion and the place designated for mandatory conversion of all such shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock or Series D Preferred Stock pursuant to this Section 3.3. Upon receipt of such notice, each holder of such shares of Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Preferred Stock converted pursuant to Section 3.3(i)(i), including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the time of the Special Mandatory Conversion (notwithstanding the failure of the holder or holders thereof to surrender the certificates for such shares at or prior to such time), except only the rights of the holders thereof, upon surrender of their certificate or certificates therefor (or lost certificate affidavit and agreement), to receive the items provided for in the next sentence of this Section 3.3(i)(ii). As soon as practicable after the Special Mandatory Conversion and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Preferred Stock so converted, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Section 3.3(c) in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends on the shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock converted. Such converted Seed

Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Seed Preferred Stock, Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series D Preferred Stock accordingly.

(iii) Definitions. For purposes of this Section 3.3(i), the following definitions shall apply:

(1) "Affiliate" shall mean, with respect to any holder of shares of Preferred Stock, (i) any person, entity or firm which, directly or indirectly, controls, is controlled by or is under common control with such holder, (ii) any entity of which such holder is a partner or member, (iii) any partner, officer, director, member or employee of such holder, (iv) any partner, officer, director, member or employee of an Affiliate of such holder and (v) any venture capital fund now or hereafter existing (x) of which such holder is a partner or member, (y) which is controlled by or under common control with one or more general partners of such holder, or (z) shares the same management company with such holder.

(2) "Offered Securities" shall mean the equity securities, or debt securities convertible (whether directly or indirectly) into equity securities, of the Corporation set aside by the Board of Directors of the Corporation for purchase by holders of outstanding shares of Preferred Stock in connection with a Qualified Financing, and offered to such holders.

(3) "Pro Rata Amount" shall mean, with respect to any holder of Preferred Stock, the lesser of (a) a number of Offered Securities calculated by multiplying the aggregate number of Offered Securities by a fraction, the numerator of which is equal to the number of shares of Common Stock issuable upon conversion of all shares of Preferred Stock (i) then owned by such holder and (ii) issuable to such holder upon exercise of any warrants to purchase shares of Preferred Stock then owned by such holder, and the denominator of which is equal to the aggregate number of shares of Common Stock issuable upon conversion of all shares of Preferred Stock (i) then owned by all holders of Preferred Stock and (ii) issuable to all holders of Preferred Stock upon exercise of any warrants to purchase shares of Preferred Stock then owned by all such holders, or (b) the maximum number of Offered Securities that such holder is permitted by the Corporation to purchase in such Qualified Financing, after giving effect to any cutbacks or limitations established by the Board of Directors and applied on a pro rata basis to all holders of Preferred Stock.

(4) “Qualified Financing” shall mean any transaction involving the issuance or sale of equity securities, or debt securities convertible (whether directly or indirectly) into equity securities, of the Corporation on or after the Second Series D Original Issue Date that is determined by the Board of Directors to be a “Qualified Financing.”

IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on the 10th day of February, 2014.

CERULEAN PHARMA INC.

By: /s/ Oliver S. Fetzer
Oliver S. Fetzer
President and Chief Executive Officer

CERTIFICATE OF AMENDMENT
OF
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Cerulean Pharma Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the “Corporation”), DOES HEREBY CERTIFY AS FOLLOWS:

The Board of Directors of the Corporation duly adopted, pursuant to Sections 141 and 242 of the General Corporation Law of the State of Delaware, resolutions setting forth amendments to the Certificate of Incorporation of the Corporation and declaring said amendments advisable. The stockholders of the Corporation duly approved said proposed amendments by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolutions setting forth the amendments are as follows:

RESOLVED: That Article FOURTH, Section 3.3(b)(i) of the Certificate of Incorporation of the Corporation, as amended, be and hereby is deleted in its entirety and the following Article FOURTH, Section 3.3(b)(i) is inserted in lieu thereof:

(i) the closing of a firm commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the “Securities Act”), covering the offer and sale of Common Stock for the account of the Corporation resulting in gross proceeds to the Corporation of not less than $30,000,000 (a “Qualified IPO”); or

IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on the 21st day of March, 2014.

CERULEAN PHARMA INC.

By: /s/ Oliver S. Fetzer
Oliver S. Fetzer
President and Chief Executive Officer

CERTIFICATE OF AMENDMENT
OF
AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Pursuant to Section 242 of the
General Corporation Law of the State of Delaware

Cerulean Pharma Inc. (hereinafter called the "Corporation"), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware, does hereby certify as follows:

A resolution was duly adopted by the Board of Directors of the Corporation pursuant to Section 242 of the General Corporation Law of the State of Delaware setting forth an amendment to the Amended and Restated Certificate of Incorporation of the Corporation, as amended, and declaring said amendment to be advisable. The stockholders of the Corporation duly approved said proposed amendment by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolutions setting forth the amendment are as follows:

RESOLVED: That new first and second paragraphs of Article FOURTH, Section 1 of the Amended and Restated Certificate of Incorporation of the Corporation, as amended, be and hereby are inserted immediately preceding the existing first paragraph (listing the authorized shares of stock of the Corporation):

"FOURTH. That, effective on the filing of this Certificate of Amendment to the Certificate of Incorporation with the Secretary of State of the State of Delaware (the "Effective Time"), a one-for-11.3426 reverse stock split of the Corporation's common stock, par value $0.0001 per share (the "Common Stock"), shall become effective, pursuant to which each 11.3426 shares of Common Stock outstanding and held of record by each stockholder of the Corporation (including treasury shares) immediately prior to the Effective Time shall be reclassified and combined into one validly issued, fully paid and nonassessable share of Common Stock automatically and without any action by the holder thereof upon the Effective Time and shall represent one share of Common Stock from and after the Effective Time (such reclassification and combination of shares, the "Reverse Stock Split"). The par value of the Common Stock following the Reverse Stock Split shall remain at $0.0001 per share. No fractional shares of Common Stock shall be issued as a result of the Reverse Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Reverse Stock Split, following the

Effective Time, shall be entitled to receive a cash payment equal to the fraction of a share of Common Stock to which such holder would otherwise be entitled multiplied by the fair value per share of the Common Stock immediately prior to the Effective Time as determined by the Board of Directors of the Corporation.

Each stock certificate that, immediately prior to the Effective Time, represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall, from and after the Effective Time, automatically and without the necessity of presenting the same for exchange, represent that number of whole shares of Common Stock after the Effective Time into which the shares formerly represented by such certificate have been reclassified (as well as the right to receive cash in lieu of fractional shares of Common Stock after the Effective Time); provided, however, that each person of record holding a certificate that represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall receive, upon surrender of such certificate, a new certificate evidencing and representing the number of whole shares of Common Stock after the Effective Time into which the shares of Common Stock formerly represented by such certificate shall have been reclassified.

RESOLVED: That Section 3.3(d)(i)(4)(B) of Article FOURTH of the Certificate of Incorporation of the Corporation, as amended, be and hereby is amended by deleting the number “18,500,000” and inserting in lieu thereof “1,631,020”.

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IN WITNESS WHEREOF, the Corporation has caused its corporate seal to be affixed hereto and this Certificate of Amendment to be signed by its President and Chief Executive Officer this 28th day of March, 2014.

CERULEAN PHARMA INC.

By: /s/ Oliver S. Fetzer
Oliver S. Fetzer
President and Chief Executive Officer

CERTIFICATE OF AMENDMENT
OF
AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Pursuant to Section 242 of the
General Corporation Law of the State of Delaware

Cerulean Pharma Inc. (hereinafter called the “Corporation”), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware, does hereby certify as follows:

A resolution was duly adopted by the Board of Directors of the Corporation pursuant to Section 242 of the General Corporation Law of the State of Delaware setting forth an amendment to the Amended and Restated Certificate of Incorporation of the Corporation, as amended, and declaring said amendment to be advisable. The stockholders of the Corporation duly approved said proposed amendment by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolutions setting forth the amendment are as follows:

RESOLVED: That the first and second paragraphs of Article FOURTH, Section 1 of the Amended and Restated Certificate of Incorporation of the Corporation, as amended, be and hereby are deleted in their entirety and the following paragraphs are inserted in lieu thereof:

“FOURTH. That, effective on the filing of this Certificate of Amendment to the Certificate of Incorporation with the Secretary of State of the State of Delaware (the “Effective Time”), a 11.3426-for-one forward stock split of the Corporation’s common stock, par value $0.0001 per share (the “Common Stock”), shall become effective, pursuant to which each one share of the Common Stock outstanding and held of record by each stockholder of the Corporation (including treasury shares) immediately prior to the Effective Time shall be reclassified into 11.3426 shares of Common Stock automatically and without any action by the holder thereof upon the Effective Time and shall represent 11.3426 shares of Common Stock from and after the Effective Time (such reclassification and combination of shares, the “Forward Stock Split”). The par value of the Common Stock following the Forward Stock Split shall remain at $0.0001 per share. No fractional shares of Common Stock shall be issued as a result of the Forward Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Forward Stock Split, following the Effective Time, shall be entitled to receive a cash payment equal to the fraction of a share of Common Stock to which such holder would otherwise be entitled multiplied by the fair value per share of the Common Stock immediately prior to the Effective Time as determined by the Board of Directors of the Corporation.

Each stock certificate that, immediately prior to the Effective Time, represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall, from and after the Effective Time, automatically and without the necessity of presenting the same for exchange, represent that number of whole shares of Common Stock after the Effective Time into which the shares formerly represented by such certificate have been reclassified (as well as the right to receive cash in lieu of fractional shares of Common Stock after the Effective Time).

RESOLVED: That Section 3.3(d)(i)(4)(B) of Article FOURTH of the Certificate of Incorporation of the Corporation, as amended, be and hereby is amended by deleting the number “1,275,212” and inserting in lieu thereof “18,500,000”.

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IN WITNESS WHEREOF, the Corporation has caused its corporate seal to be affixed hereto and this Certificate of Amendment to be signed by its President and Chief Executive Officer this 31st day of March, 2014.

CERULEAN PHARMA INC.

By: /s/ Oliver S. Fetzer
Oliver S. Fetzer
President and Chief Executive Officer

CERTIFICATE OF AMENDMENT
OF
AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
CERULEAN PHARMA INC.

Pursuant to Section 242 of the
General Corporation Law of the State of Delaware

Cerulean Pharma Inc. (hereinafter called the “Corporation”), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware, does hereby certify as follows:

A resolution was duly adopted by the Board of Directors of the Corporation pursuant to Section 242 of the General Corporation Law of the State of Delaware setting forth an amendment to the Amended and Restated Certificate of Incorporation of the Corporation, as amended, and declaring said amendment to be advisable. The stockholders of the Corporation duly approved said proposed amendment by written consent in accordance with Sections 228 and 242 of the General Corporation Law of the State of Delaware. The resolutions setting forth the amendment are as follows:

RESOLVED: That first and second paragraphs of Article FOURTH, Section 1 of the Amended and Restated Certificate of Incorporation of the Corporation, as amended, be and hereby are deleted in their entirety and the following paragraphs are inserted in lieu thereof:

“FOURTH. That, effective on the filing of this Certificate of Amendment to the Certificate of Incorporation with the Secretary of State of the State of Delaware (the “Effective Time”), a one-for-14.5074 reverse stock split of the Corporation’s common stock, par value $0.0001 per share (the “Common Stock”), shall become effective, pursuant to which each 14.5074 shares of Common Stock outstanding and held of record by each stockholder of the Corporation (including treasury shares) immediately prior to the Effective Time shall be reclassified and combined into one validly issued, fully paid and nonassessable share of Common Stock automatically and without any action by the holder thereof upon the Effective Time and shall represent one share of Common Stock from and after the Effective Time (such reclassification and combination of shares, the “Reverse Stock Split”). The par value of the Common Stock following the Reverse Stock Split shall remain at $0.0001 per share. No fractional shares of Common Stock shall be issued as a result of the Reverse Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Reverse Stock Split, following the Effective Time, shall be entitled to receive a cash payment equal to the fraction of a share of Common Stock to which such holder would otherwise be entitled multiplied by the fair value per share of the Common Stock immediately prior to the Effective Time as determined by the Board of Directors of the Corporation.

Each stock certificate that, immediately prior to the Effective Time, represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall, from and after the Effective Time, automatically and without the necessity of presenting the same for exchange, represent that number of whole shares of Common Stock after the Effective Time into which the shares formerly represented by such certificate have been reclassified (as well as the right to receive cash in lieu of fractional shares of Common Stock after the Effective Time); provided, however, that each person of record holding a certificate that represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall receive, upon surrender of such certificate, a new certificate evidencing and representing the number of whole shares of Common Stock after the Effective Time into which the shares of Common Stock formerly represented by such certificate shall have been reclassified.

RESOLVED: That Section 3.3(d)(i)(4)(B) of Article FOURTH of the Certificate of Incorporation of the Corporation, as amended, be and hereby is amended by deleting the number “18,500,000” and inserting in lieu thereof “1,275,212”.

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IN WITNESS WHEREOF, the Corporation has caused its corporate seal to be affixed hereto and this Certificate of Amendment to be signed by its President and Chief Executive Officer this 31st day of March, 2014.

CERULEAN PHARMA INC.

By: /s/ Oliver S. Fetzer
Oliver S. Fetzer
President and Chief Executive Officer

Exhibit 4.1

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CERULEAN™

CERULEAN PHARMA INC.

INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

CUSIP 157080 10 5
SEE REVERSE FOR CERTAIN DEFINITIONS

THIS CERTIFIES THAT

SPECIMEN

IS THE RECORD HOLDER OF

FULLY PAID AND NON-ASSESSABLE SHARES OF COMMON STOCK $0.0001 PAR VALUE PER SHARE, OF

CERULEAN PHARMA INC.

transferable on the books of the Corporation in person or by duly authorized attorney upon surrender of the certificate properly endorsed.

This certificate is not valid until countersigned by the Transfer Agent and Registered by the Registrar.

WITNESS the facsimile seal of the Corporation and the facsimile signatures of its duly authorized officers.

Dated

2005

PRESIDENT

Karen L Roberts
TREASURER

COUNTERSIGNED AND REGISTERED:
AMERICAN STOCK TRANSFER & TRUST COMPANY, LLC
(Brooklyn, NY)
TRANSFER AGENT
AND REGISTRAR

BY:

AUTHORIZED SIGNATURE

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM	–	as tenants in common
TEN ENT	–	as tenants by the entireties
JT TEN	–	as joint tenants with right of survivorship and not as tenants in common

UNIF GIFT MIN ACT– __________ Custodian __________
(Cust) (Minor)
under Uniform Gifts to Minors
Act ____________________
(State)

Additional abbreviations may also be used though not in the above list.

For Value Received, ______________________________________ hereby sell, assign and transfer unto

PLEASE INSERT SOCIAL SECURITY OR OTHER
IDENTIFYING NUMBER OF ASSIGNEE

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS OF ASSIGNEE)

Shares of the common stock represented by the within Certificate, and do hereby irrevocably constitute and appoint

Attorney to transfer the said stock on the books of the within named Corporation with full power of substitution in the premises.

Dated ______________________________________

X ______________________________________

X ______________________________________

NOTICE: THE SIGNATURE TO THIS ASSIGNMENT MUST CORRESPOND WITH THE NAME AS WRITTEN UPON THE FACE OF THE CERTIFICATE IN EVERY PARTICULAR,
WITHOUT ALTERATION OR ENLARGEMENT OR ANY CHANGE WHATEVER.

Signature(s) Guaranteed:

THE SIGNATURE(S) MUST BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (BANKS, STOCKBROKERS, SAVINGS AND LOAN ASSOCIATIONS AND CREDIT UNIONS WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM), PURSUANT TO S.E.C. RULE 17Ad-15.

Exhibit 5.1

WILMERHALE

March 31, 2014

+1 617 526 6000(t)
+1 617 526 5000(f)
wilmerhale.com

Cerulean Pharma Inc.
840 Memorial Drive
Cambridge, MA 02139

Re: Registration Statement on Form S-1

Ladies and Gentlemen:

This opinion is furnished to you in connection with a Registration Statement on Form S-1 (File No. 333-194442) (the “Registration Statement”) filed with the Securities and Exchange Commission (the “Commission”) under the Securities Act of 1933, as amended (the “Securities Act”), for the registration of shares of Common Stock, par value $0.0001 per share, of Cerulean Pharma Inc., a Delaware corporation (the “Company”), with a proposed maximum aggregate offering price of $74,750,000 (the “Shares”), including Shares issuable upon exercise of an over-allotment option granted by the Company.

The Shares are to be sold by the Company pursuant to an underwriting agreement (the “Underwriting Agreement”) to be entered into by and among the Company and Leerink Partners LLC, as representative of the several underwriters named in the Underwriting Agreement, the form of which has been filed as Exhibit 1.1 to the Registration Statement.

We are acting as counsel for the Company in connection with the issue and sale by the Company of the Shares. We have examined signed copies of the Registration Statement as filed with the Commission. We have also examined and relied upon the Underwriting Agreement, minutes of meetings of the stockholders and the Board of Directors of the Company as provided to us by the Company, stock record books of the Company as provided to us by the Company, the Certificate of Incorporation and By-Laws of the Company, each as restated and/or amended to date, and such other documents as we have deemed necessary for purposes of rendering the opinions hereinafter set forth.

In our examination of the foregoing documents, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as copies, the authenticity of the originals of such latter documents and the legal competence of all signatories to such documents.

We express no opinion herein as to the laws of any state or jurisdiction other than the state laws of the Commonwealth of Massachusetts, the General Corporation Law of the State of Delaware and the federal laws of the United States of America.

Based upon and subject to the foregoing, we are of the opinion that the Shares have been duly authorized for issuance and, when the Shares are issued and paid for in accordance with the terms and conditions of the Underwriting Agreement, the Shares will be validly issued, fully paid and nonassessable.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

We hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act and to the use of our name therein and in the related Prospectus under the caption “Legal matters.” In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Sincerely,

WILMER CUTLER PICKERING HALE AND DORR LLP

By: /s/ Lia Der Marderosian
Lia Der Marderosian, Partner

Exhibit 10.4

CERULEAN PHARMA INC.

2014 STOCK INCENTIVE PLAN

1. Purpose

The purpose of this 2014 Stock Incentive Plan (the “***Plan***”) of Cerulean Pharma Inc., a Delaware corporation (the “***Company***”), is to advance the interests of the Company’s stockholders by enhancing the Company’s ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities and performance-based incentives that are intended to better align the interests of such persons with those of the Company’s stockholders. Except where the context otherwise requires, the term “***Company***” shall include any of the Company’s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Internal Revenue Code of 1986, as amended, and any regulations thereunder (the “***Code***”) and any other business venture (including, without limitation, joint venture or limited liability company) in which the Company has a controlling interest, as determined by the Board of Directors of the Company (the “***Board***”).

2. Eligibility

All of the Company’s employees, officers and directors, as well as consultants and advisors to the Company (as the terms consultants and advisors are defined and interpreted for purposes of Form S-8 under the Securities Act of 1933, as amended (the “***Securities Act***”), or any successor form) are eligible to be granted Awards under the Plan. Each person who is granted an Award under the Plan is deemed a “***Participant***.” “***Award***” means Options (as defined in Section 5), SARs (as defined in Section 6), Restricted Stock (as defined in Section 7), Restricted Stock Units (as defined in Section 7) and Other Stock-Based Awards (as defined in Section 8).

3. Administration and Delegation

(a) Administration by Board of Directors. The Plan will be administered by the Board. The Board shall have authority to grant Awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the Plan as it shall deem advisable. The Board may construe and interpret the terms of the Plan and any Award agreements entered into under the Plan. The Board may correct any defect, supply any omission or reconcile any inconsistency in the Plan or any Award in the manner and to the extent it shall deem expedient and it shall be the sole and final judge of such expediency. All decisions by the Board shall be made in the Board’s sole discretion and shall be final and binding on all persons having or claiming any interest in the Plan or in any Award.

(b) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers under the Plan to one or more committees or subcommittees of the Board (each, a “***Committee***”). All references in the Plan to the “***Board***” shall mean the Board or a Committee of the Board or the officers referred to in Section 3(c) to the extent that the Board’s powers or authority under the Plan have been delegated to such Committee or officers.

(c) Delegation to Officers. To the extent permitted by applicable law, the Board may delegate to one or more officers of the Company the power to grant Options and other Awards that constitute rights under Delaware law (subject to any limitations under the Plan) to employees or officers of the Company and to exercise such other powers under the Plan as the Board may determine, *provided* that the Board shall fix the terms of such Awards to be granted by such officers (including the exercise price of such Awards, which may include a formula by which the exercise price will be determined) and the maximum number of shares subject to such Awards that the officers may grant; *provided further*, however, that no officer shall be authorized to grant such Awards to any "executive officer" of the Company (as defined by Rule 3b-7 under the Securities Exchange Act of 1934, as amended (the "***Exchange Act***")) or to any "officer" of the Company (as defined by Rule 16a-1 under the Exchange Act). The Board may not delegate authority under this Section 3(c) to grant Restricted Stock, unless Delaware law then permits such delegation.

4. Stock Available for Awards

(a) Number of Shares; Share Counting.

(1) Authorized Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan (any or all of which Awards may be in the form of Incentive Stock Options, as defined in Section 5(b)) for up to such number of shares of common stock, $0.0001 par value per share, of the Company (the "***Common Stock***") as is equal to the sum of:

(A) 2,400,000 shares of Common Stock; plus

(B) such additional number of shares of Common Stock (up to 1,221,651 shares) as is equal to the sum of (x) the number of shares of Common Stock reserved for issuance under the Company's 2007 Stock Incentive Plan, as amended (the "***Existing Plan***"), that remain available for grant under the Existing Plan immediately prior to the closing of the Company's initial public offering and (y) the number of shares of Common Stock subject to awards granted under the Existing Plan which awards expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right (subject, however, in the case of Incentive Stock Options to any limitations of the Code); plus

(C) an annual increase to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2015 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2024, equal to the least of (i) 1,000,000 shares of Common Stock, (ii) 4% of the number of outstanding shares of Common Stock on such date or (iii) an amount determined by the Board.

Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

(2) Share Counting. For purposes of counting the number of shares available for the grant of Awards under the Plan:

(A) all shares of Common Stock covered by SARs shall be counted against the number of shares available for the grant of Awards under the Plan; *provided, however*, that (i) SARs that may be settled only in cash shall not be so counted and (ii) if the Company grants an SAR in tandem with an Option for the same number of shares of Common Stock and provides that only one such Award may be exercised (a "***Tandem SAR***"), only the shares covered by the Option, and not the shares covered by the Tandem SAR, shall be so counted, and the expiration of one in connection with the other's exercise will not restore shares to the Plan;

(B) if any Award (i) expires or is terminated, surrendered or canceled without having been fully exercised or is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right) or (ii) results in any Common Stock not being issued (including as a result of an SAR that was settleable either in cash or in stock actually being settled in cash), the unused Common Stock covered by such Award shall again be available for the grant of Awards; *provided, however*, that (1) in the case of Incentive Stock Options, the foregoing shall be subject to any limitations under the Code, (2) in the case of the exercise of an SAR, the number of shares counted against the shares available under the Plan shall be the full number of shares subject to the SAR multiplied by the percentage of the SAR actually exercised, regardless of the number of shares actually used to settle such SAR upon exercise and (3) the shares covered by a Tandem SAR shall not again become available for grant upon the expiration or termination of such Tandem SAR; and

(C) shares of Common Stock delivered (either by actual delivery, attestation, or net exercise) to the Company by a Participant to (i) purchase shares of Common Stock upon the exercise of an Award or (ii) satisfy tax withholding obligations (including shares retained from the Award creating the tax obligation) shall not be added back to the number of shares available for the future grant of Awards.

(b) Substitute Awards. In connection with a merger or consolidation of an entity with the Company or the acquisition by the Company of property or stock of an entity, the Board may grant Awards in substitution for any options or other stock or stock-based awards granted by such entity or an affiliate thereof. Substitute Awards may be granted on such terms as the Board deems appropriate in the circumstances, notwithstanding any limitations on Awards contained in the Plan. Substitute Awards shall not count against the overall share limit set forth in Section 4(a)(1), except as may be required by reason of Section 422 and related provisions of the Code.

5. Stock Options

(a) General. The Board may grant options to purchase Common Stock (each, an "***Option***") and determine the number of shares of Common Stock to be covered by each Option, the exercise price of each Option and the conditions and limitations applicable to the exercise of each Option, including conditions relating to applicable federal or state securities laws, as it considers necessary or advisable.

(b) Incentive Stock Options. An Option that the Board intends to be an "incentive stock option" as defined in Section 422 of the Code (an "***Incentive Stock Option***") shall only be granted to employees of Cerulean Pharma Inc., any of Cerulean Pharma Inc.'s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code, and any other entities the employees of which are eligible to receive Incentive Stock Options under the Code, and shall be subject to and shall be construed consistently with the requirements of Section 422 of the Code. An Option that is not intended to be an Incentive Stock Option shall be designated a "***Nonstatutory Stock Option***." The Company shall have no liability to a Participant, or any other party, if an Option (or any part thereof) that is intended to be an Incentive Stock Option is not an Incentive Stock Option or if the Company converts an Incentive Stock Option to a Nonstatutory Stock Option.

(c) Exercise Price. The Board shall establish the exercise price of each Option and specify the exercise price in the applicable Option agreement. The exercise price shall be not less than 100% of the fair market value per share of Common Stock as determined by (or in a manner approved by) the Board ("***Fair Market Value***") on the date the Option is granted; *provided* that if the Board approves the grant of an Option with an exercise price to be determined on a future date, the exercise price shall be not less than 100% of the Fair Market Value on such future date.

(d) Duration of Options. Each Option shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable option agreement; *provided, however,* that no Option will be granted with a term in excess of 10 years.

(e) Exercise of Options. Options may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with payment in full (in the manner specified in Section 5(f)) of the exercise price for the number of shares for which the Option is exercised. Shares of Common Stock subject to the Option will be delivered by the Company as soon as practicable following exercise.

(f) Payment Upon Exercise. Common Stock purchased upon the exercise of an Option granted under the Plan shall be paid for as follows:

(1) in cash or by check, payable to the order of the Company;

(2) except as may otherwise be provided in the applicable Option agreement or approved by the Board, in its sole discretion, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker to deliver promptly to the Company cash or a check sufficient to pay the exercise price and any required tax withholding;

(3) to the extent provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their Fair Market Value, provided (i) such method of payment is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company, was owned by the Participant for such minimum period of time, if any, as may be established by the Board in its discretion and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

(4) to the extent provided for in the applicable Nonstatutory Stock Option agreement or approved by the Board in its sole discretion, by delivery of a notice of "net exercise" to the Company, as a result of which the Participant would receive (i) the number of shares underlying the portion of the Option being exercised, less (ii) such number of shares as is equal to (A) the aggregate exercise price for the portion of the Option being exercised divided by (B) the Fair Market Value on the date of exercise;

(5) to the extent permitted by applicable law and provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by payment of such other lawful consideration as the Board may determine; or

(6) by any combination of the above permitted forms of payment.

(g) Limitation on Repricing. Unless such action is approved by the Company's stockholders, the Company may not (except as provided for under Section 9): (1) amend any outstanding Option granted under the Plan to provide an exercise price per share that is lower than the then-current exercise price per share of such outstanding Option, (2) cancel any outstanding option (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan (other than Awards granted pursuant to Section 4(b)) covering the same or a different number of shares of Common Stock and having an exercise price per share lower than the then-current exercise price per share of the cancelled option, (3) cancel in exchange for a cash payment any outstanding Option with an exercise price per share above the then-current Fair Market Value, or (4) take any other action under the Plan that constitutes a "repricing" within the meaning of the rules of the NASDAQ Stock Market ("***NASDAQ***").

6. Stock Appreciation Rights

(a) General. The Board may grant Awards consisting of stock appreciation rights ("***SARs***") entitling the holder, upon exercise, to receive an amount of Common Stock or cash or a combination thereof (such form to be determined by the Board) determined by reference to appreciation, from and after the date of grant, in the Fair Market Value of a share of Common Stock over the measurement price established pursuant to Section 6(b). The date as of which such appreciation is determined shall be the exercise date.

(b) Measurement Price. The Board shall establish the measurement price of each SAR and specify it in the applicable SAR agreement. The measurement price shall not be less than 100% of the Fair Market Value on the date the SAR is granted; *provided* that if the Board approves the grant of an SAR effective as of a future date, the measurement price shall be not less than 100% of the Fair Market Value on such future date.

(c) Duration of SARs. Each SAR shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable SAR agreement; *provided, however*, that no SAR will be granted with a term in excess of 10 years.

(d) Exercise of SARs. SARs may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with any other documents required by the Board.

(e) Limitation on Repricing. Unless such action is approved by the Company's stockholders, the Company may not (except as provided for under Section 9): (1) amend any outstanding SAR granted under the Plan to provide a measurement price per share that is lower than the then-current measurement price per share of such outstanding SAR, (2) cancel any outstanding SAR (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan (other than Awards granted pursuant to Section 4(b)) covering the same or a different number of shares of Common Stock and having an exercise or measurement price per share lower than the then-current measurement price per share of the cancelled SAR, (3) cancel in exchange for a cash payment any outstanding SAR with a measurement price per share above the then-current Fair Market Value, or (4) take any other action under the Plan that constitutes a "repricing" within the meaning of the rules of NASDAQ.

7. Restricted Stock; Restricted Stock Units

(a) General. The Board may grant Awards entitling recipients to acquire shares of Common Stock ("***Restricted Stock***"), subject to the right of the Company to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) from the recipient in the event that conditions specified by the Board in the applicable Award are not satisfied prior to the end of the applicable restriction period or periods established by the Board for such Award. The Board may also grant Awards entitling the recipient to receive shares of Common Stock or cash to be delivered at the time such Award vests ("***Restricted Stock Units***") (Restricted Stock and Restricted Stock Units are each referred to herein as a "***Restricted Stock Award***").

(b) Terms and Conditions for All Restricted Stock Awards. The Board shall determine the terms and conditions of a Restricted Stock Award, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

(c) Additional Provisions Relating to Restricted Stock.

(1) Dividends. Unless otherwise provided in the applicable Award agreement, any dividends (whether paid in cash, stock or property) declared and paid by the Company with respect to shares of Restricted Stock ("***Accrued Dividends***") shall be paid to the Participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. Each payment of Accrued Dividends will be made no later than the end of the calendar year in which the dividends are paid to stockholders of that class of stock or, if later, the 15th day of the third month following the lapsing of the restrictions on transferability and the forfeitability provisions applicable to the underlying shares of Restricted Stock.

(2) Stock Certificates. The Company may require that any stock certificates issued in respect of shares of Restricted Stock, as well as dividends or distributions paid on such Restricted Stock, shall be deposited in escrow by the Participant, together with a stock power endorsed in blank, with the Company (or its designee). At the expiration of the applicable restriction periods, the Company (or such designee) shall deliver the certificates no longer subject to such restrictions to the Participant or if the Participant has died, to his or her Designated Beneficiary. "***Designated Beneficiary***" means (i) the beneficiary designated, in a

manner determined by the Board, by a Participant to receive amounts due or exercise rights of the Participant in the event of the Participant's death or (ii) in the absence of an effective designation by a Participant, the Participant's estate.

(d) Additional Provisions Relating to Restricted Stock Units.

(1) Settlement. Upon the vesting of and/or lapsing of any other restrictions (i.e., settlement) with respect to each Restricted Stock Unit, the Participant shall be entitled to receive from the Company such number of shares of Common Stock or (if so provided in the applicable Award agreement) an amount of cash equal to the Fair Market Value of such number of shares of Common Stock as set forth in the applicable Award agreement. The Board may, in its discretion, provide that settlement of Restricted Stock Units shall be deferred, on a mandatory basis or at the election of the Participant in a manner that complies with Section 409A of the Code.

(2) Voting Rights. A Participant shall have no voting rights with respect to any Restricted Stock Units.

(3) Dividend Equivalents. The Award agreement for Restricted Stock Units may provide Participants with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of Common Stock ("***Dividend Equivalents***"). Dividend Equivalents may be paid currently or credited to an account for the Participant, may be settled in cash and/or shares of Common Stock and may be subject to the same restrictions on transfer and forfeitability as the Restricted Stock Units with respect to which paid, in each case to the extent provided in the Award agreement.

8. Other Stock-Based Awards

(a) General. Other Awards of shares of Common Stock, and other Awards that are valued in whole or in part by reference to, or are otherwise based on, shares of Common Stock or other property, may be granted hereunder to Participants ("***Other Stock-Based-Awards***"). Such Other Stock-Based Awards shall also be available as a form of payment in the settlement of other Awards granted under the Plan or as payment in lieu of compensation to which a Participant is otherwise entitled. Other Stock-Based Awards may be paid in shares of Common Stock or cash, as the Board shall determine.

(b) Terms and Conditions. Subject to the provisions of the Plan, the Board shall determine the terms and conditions of each Other Stock-Based Award, including any purchase price applicable thereto.

9. Adjustments for Changes in Common Stock and Certain Other Events

(a) Changes in Capitalization. In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under the Plan, (ii) the share counting rules set forth in Section 4(a), (iii) the number and class of securities and exercise price per share of each outstanding Option, (iv) the share and per-share provisions and the measurement price of each outstanding SAR, (v) the number of shares subject to and the repurchase price per share subject to each outstanding Restricted Stock Award and (vi) the share and per-share-related provisions and the purchase price, if any, of each outstanding Other Stock-Based Award, shall be equitably adjusted by the Company (or substituted Awards may be made, if applicable) in the manner determined by the Board. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to an outstanding Option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then an optionee who exercises an Option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon such Option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

(b) Reorganization Events.

(1) Definition. A "***Reorganization Event***" shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Awards Other than Restricted Stock.

(A) In connection with a Reorganization Event, the Board may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards other than Restricted Stock on such terms as the Board determines (except to the extent specifically provided otherwise in an applicable Award agreement or another agreement between the Company and the Participant): (i) provide that such Awards shall be assumed, or substantially equivalent Awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) upon written notice to a Participant, provide that all of the Participant's unvested and/or unexercised Awards will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant (to the extent then exercisable) within a specified period following the date of such notice, (iii) provide that outstanding Awards shall become exercisable, realizable, or deliverable, or restrictions applicable to an Award shall lapse, in whole or in part prior to or upon such Reorganization Event, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the "***Acquisition Price***"), make or provide for a cash payment to Participants with respect to each Award held by a Participant equal to (A) the number of shares of Common Stock subject to the vested portion of the Award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such Reorganization Event) multiplied by (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise, measurement or purchase price of such Award and any applicable tax withholdings, in exchange for the termination of such Award, (v) provide that, in connection with a liquidation or dissolution of the Company, Awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing. In taking any of the actions permitted under this Section 9(b)(2), the Board shall not be obligated by the Plan to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically.

(B) Notwithstanding the terms of Section 9(b)(2)(A), in the case of outstanding Restricted Stock Units that are subject to Section 409A of the Code: (i) if the applicable Restricted Stock Unit agreement provides that the Restricted Stock Units shall be settled upon a “change in control event” within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i), and the Reorganization Event constitutes such a “change in control event”, then no assumption or substitution shall be permitted pursuant to Section 9(b)(2)(A)(i) and the Restricted Stock Units shall instead be settled in accordance with the terms of the applicable Restricted Stock Unit agreement; and (ii) the Board may only undertake the actions set forth in clauses (iii), (iv) or (v) of Section 9(b)(2)(A) if the Reorganization Event constitutes a “change in control event” as defined under Treasury Regulation Section 1.409A-3(i)(5)(i) and such action is permitted or required by Section 409A of the Code; if the Reorganization Event is not a “change in control event” as so defined or such action is not permitted or required by Section 409A of the Code, and the acquiring or succeeding corporation does not assume or substitute the Restricted Stock Units pursuant to clause (i) of Section 9(b)(2)(A), then the unvested Restricted Stock Units shall terminate immediately prior to the consummation of the Reorganization Event without any payment in exchange therefor.

(C) For purposes of Section 9(b)(2)(A)(i), an Award (other than Restricted Stock) shall be considered assumed if, following consummation of the Reorganization Event, such Award confers the right to purchase or receive pursuant to the terms of such Award, for each share of Common Stock subject to the Award immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); *provided, however*, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise or settlement of the Award to consist solely of such number of shares of common stock of the acquiring or succeeding corporation (or an affiliate thereof) that the Board determined to be equivalent in value (as of the date of such determination or another date specified by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

(3) <u>Consequences of a Reorganization Event on Restricted Stock</u>. Upon the occurrence of a Reorganization Event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company with respect to outstanding Restricted Stock shall inure to the benefit of the Company’s successor and shall, unless the Board determines otherwise, apply to the cash, securities or other property which the Common Stock was converted into or exchanged for pursuant to such Reorganization Event in the same manner and

to the same extent as they applied to such Restricted Stock; *provided*, *however*, that the Board may provide for termination or deemed satisfaction of such repurchase or other rights under the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, either initially or by amendment. Upon the occurrence of a Reorganization Event involving the liquidation or dissolution of the Company, except to the extent specifically provided to the contrary in the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, all restrictions and conditions on all Restricted Stock then outstanding shall automatically be deemed terminated or satisfied.

10. General Provisions Applicable to Awards

(a) Transferability of Awards. Awards shall not be sold, assigned, transferred, pledged or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution or, other than in the case of an Incentive Stock Option, pursuant to a qualified domestic relations order, and, during the life of the Participant, shall be exercisable only by the Participant; *provided*, *however*, that the Board may permit or provide in an Award for the gratuitous transfer of the Award by the Participant to or for the benefit of any immediate family member, family trust or other entity established for the benefit of the Participant and/or an immediate family member thereof if the Company would be eligible to use a Form S-8 under the Securities Act for the registration of the sale of the Common Stock subject to such Award to such proposed transferee; *provided further*, that the Company shall not be required to recognize any such permitted transfer until such time as such permitted transferee shall, as a condition to such transfer, deliver to the Company a written instrument in form and substance satisfactory to the Company confirming that such transferee shall be bound by all of the terms and conditions of the Award. References to a Participant, to the extent relevant in the context, shall include references to authorized transferees. For the avoidance of doubt, nothing contained in this Section 10(a) shall be deemed to restrict a transfer to the Company.

(b) Documentation. Each Award shall be evidenced in such form (written, electronic or otherwise) as the Board shall determine. Each Award may contain terms and conditions in addition to those set forth in the Plan.

(c) Board Discretion. Except as otherwise provided by the Plan, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award need not be identical, and the Board need not treat Participants uniformly.

(d) Termination of Status. The Board shall determine the effect on an Award of the disability, death, termination or other cessation of employment, authorized leave of absence or other change in the employment or other status of a Participant and the extent to which, and the period during which, the Participant, or the Participant's legal representative, conservator, guardian or Designated Beneficiary, may exercise rights under the Award.

(e) Withholding. The Participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before the Company will deliver stock certificates or otherwise recognize ownership of Common Stock under an Award. The Company may decide to satisfy the withholding obligations through additional withholding on salary or wages. If the Company elects not to or cannot withhold from other compensation, the Participant must pay the Company the full amount, if any, required for withholding or have a broker tender to the Company cash equal to the withholding obligations. Payment of withholding obligations is due before the Company will issue any shares on exercise, vesting or release from forfeiture of an Award or at the same time as payment of the exercise or purchase price, unless the Company determines otherwise. If provided for in an Award or approved by the Board in its sole discretion, a Participant may satisfy such tax obligations in whole or in part by delivery (either by actual delivery or attestation) of shares of Common Stock, including shares retained from the Award creating the tax obligation, valued at their Fair Market Value; *provided, however*, except as otherwise provided by the Board, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed the Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income). Shares used to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements.

(f) Amendment of Award. Except as otherwise provided in Sections 5(g) and 6(e) with respect to repricings and Section 11(d) with respect to actions requiring stockholder approval, the Board may amend, modify or terminate any outstanding Award, including but not limited to, substituting therefor another Award of the same or a different type, changing the date of exercise or realization, and converting an Incentive Stock Option to a Nonstatutory Stock Option. The Participant's consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, does not materially and adversely affect the Participant's rights under the Plan or (ii) the change is permitted under Section 9.

(g) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to the Plan or to remove restrictions from shares previously issued or delivered under the Plan until (i) all conditions of the Award have been met or removed to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been satisfied, including any applicable securities laws and regulations and any applicable stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations.

(h) Acceleration. The Board may at any time provide that any Award shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

11. Miscellaneous

(a) No Right To Employment or Other Status. No person shall have any claim or right to be granted an Award by virtue of the adoption of the Plan, and the grant of an Award shall not be construed as giving a Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan, except as expressly provided in the applicable Award.

(b) No Rights As Stockholder. Subject to the provisions of the applicable Award, no Participant or Designated Beneficiary shall have any rights as a stockholder with respect to any shares of Common Stock to be distributed with respect to an Award until becoming the record holder of such shares.

(c) Effective Date and Term of Plan. The Plan shall become effective on the date the Plan is approved by the Company's stockholders (the "***Effective Date***"). No Awards shall be granted under the Plan after the expiration of 10 years from the Effective Date, but Awards previously granted may extend beyond that date.

(d) Amendment of Plan. The Board may amend, suspend or terminate the Plan or any portion thereof at any time provided that (i) to the extent required by Section 162(m) of the Code, no Award granted to a Participant that is intended to comply with Section 162(m) of the Code after the date of such amendment shall become exercisable, realizable or vested, as applicable to such Award, unless and until the Company's stockholders approve such amendment in the manner required by Section 162(m) of the Code; and (ii) no amendment that would require stockholder approval under the rules of NASDAQ may be made effective unless and until the Company's stockholders approve such amendment. In addition, if at any time the approval of the Company's stockholders is required as to any other modification or amendment under Section 422 of the Code or any successor provision with respect to Incentive Stock Options, the Board may not effect such modification or amendment without such approval. Unless otherwise specified in the amendment, any amendment to the Plan adopted in accordance with this Section 11(d) shall apply to, and be binding on the holders of, all Awards outstanding under the Plan at the time the amendment is adopted, provided the Board determines that such amendment, taking into account any related action, does not materially and adversely affect the rights of Participants under the Plan. No Award shall be made that is conditioned upon stockholder approval of any amendment to the Plan unless the Award provides that (i) it will terminate or be forfeited if stockholder approval of such amendment is not obtained within no more than 12 months from the date of grant and (2) it may not be exercised or settled (or otherwise result in the issuance of Common Stock) prior to such stockholder approval.

(e) Authorization of Sub-Plans (including for Grants to non-U.S. Employees). The Board may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The Board shall establish such sub-plans by adopting supplements to the Plan containing (i) such limitations on the Board's discretion under the Plan as the Board deems necessary or desirable or (ii) such additional terms and conditions not otherwise inconsistent with the Plan as the Board shall deem necessary or desirable. All supplements adopted by the Board shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction which is not the subject of such supplement.

(f) Compliance with Section 409A of the Code. Except as provided in individual Award agreements initially or by amendment, if and to the extent (i) any portion of any payment, compensation or other benefit provided to a Participant pursuant to the Plan in connection with his or her employment termination constitutes “nonqualified deferred compensation” within the meaning of Section 409A of the Code and (ii) the Participant is a specified employee as defined in Section 409A(a)(2)(B)(i) of the Code, in each case as determined by the Company in accordance with its procedures, by which determinations the Participant (through accepting the Award) agrees that he or she is bound, such portion of the payment, compensation or other benefit shall not be paid before the day that is six months plus one day after the date of “separation from service” (as determined under Section 409A of the Code) (the “***New Payment Date***”), except as Section 409A of the Code may then permit. The aggregate of any payments that otherwise would have been paid to the Participant during the period between the date of separation from service and the New Payment Date shall be paid to the Participant in a lump sum on such New Payment Date, and any remaining payments will be paid on their original schedule.

The Company makes no representations or warranty and shall have no liability to the Participant or any other person if any provisions of or payments, compensation or other benefits under the Plan are determined to constitute nonqualified deferred compensation subject to Section 409A of the Code but do not to satisfy the conditions of that section.

(g) Limitations on Liability. Notwithstanding any other provisions of the Plan, no individual acting as a director, officer, employee or agent of the Company will be liable to any Participant, former Participant, spouse, beneficiary, or any other person for any claim, loss, liability, or expense incurred in connection with the Plan, nor will such individual be personally liable with respect to the Plan because of any contract or other instrument he or she executes in his or her capacity as a director, officer, employee or agent of the Company. The Company will indemnify and hold harmless each director, officer, employee or agent of the Company to whom any duty or power relating to the administration or interpretation of the Plan has been or will be delegated, against any cost or expense (including attorneys’ fees) or liability (including any sum paid in settlement of a claim with the Board’s approval) arising out of any act or omission to act concerning the Plan unless arising out of such person’s own fraud or bad faith.

(h) Governing Law. The provisions of the Plan and all Awards made hereunder shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than the State of Delaware.

Exhibit 10.5

CERULEAN PHARMA INC.

INCENTIVE STOCK OPTION AGREEMENT
GRANTED UNDER 2014 STOCK INCENTIVE PLAN

1. Grant of Option.

This agreement evidences the grant by Cerulean Pharma Inc., a Delaware corporation (the “Company”), on , 20 (the “Grant Date”) to (the “Participant”), of an option to purchase, in whole or in part, on the terms provided herein and in the Company’s 2014 Stock Incentive Plan (the “Plan”), a total of shares (the “Shares”) of common stock, par value $0.0001 per share, of the Company (“Common Stock”) at a price of $ per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on (the “Final Exercise Date”).

It is intended that the option evidenced by this agreement shall be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the “Code”). Except as otherwise indicated by the context, the term “Participant”, as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable (“vest”) as follows: .

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be in writing in the Form of Notice of Stock Option Exercise attached hereto, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or by such other method as shall be approved by the Company, in any case together with payment in full in the manner provided in the Plan. The Participant may exercise this option for less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee or officer or director of, or consultant or advisor (as such terms are defined and interpreted for purposes of Form S-8 under the Securities Act of 1933, as amended) to, the Company or any parent or subsidiary of the Company as defined in Section 424(e) or (f) of the Code (an “Eligible Participant”).

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon written notice to the Participant from the Company describing such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for “cause” as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant’s employment is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment by the Company for Cause, and the effective date of such employment termination is subsequent to the date of delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant’s employment shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate upon the effective date of such termination of employment). If the Participant is party to an employment or severance agreement with the Company that contains a definition of “cause” for termination of employment, “Cause” shall have the meaning ascribed to such term in such agreement. Otherwise, “Cause” shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant’s employment shall be considered to have been terminated for Cause if the Company determines, within 30 days after the Participant’s resignation, that termination for Cause was warranted.

4. Tax Matters.

(a) Withholding. No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

(b) Disqualifying Disposition. If the Participant disposes of Shares acquired upon exercise of this option within two years from the Grant Date or one year after such Shares were acquired pursuant to exercise of this option, the Participant shall notify the Company in writing of such disposition.

5. Transfer Restrictions.

This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

6. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

[*Remainder of page intentionally left blank.*]

IN WITNESS WHEREOF, the Company has caused this option to be executed under its corporate seal by its duly authorized officer. This option shall take effect as a sealed instrument.

CERULEAN PHARMA INC.

By: ______________________________

Name: ______________________________

Title: ______________________________

[Signature Page to Incentive Stock Option Agreement]

PARTICIPANT’S ACCEPTANCE

The undersigned hereby accepts the foregoing option and agrees to the terms and conditions thereof. The undersigned hereby acknowledges receipt of a copy of the Company’s 2014 Stock Incentive Plan.

PARTICIPANT:

____

Address: ______________________________

____

FORM OF NOTICE OF STOCK OPTION EXERCISE

Date:

Cerulean Pharma Inc.
840 Memorial Drive
Cambridge, MA 02139

Attention: Treasurer

Dear Sir or Madam:

I am the holder of an Incentive Stock Option granted to me under the Cerulean Pharma Inc. (the "Company") 2014 Stock Incentive Plan on for the purchase of shares of common stock, par value $0.0001 per share, of the Company ("Common Stock") at a purchase price of $ per share.

I hereby exercise my option with respect to shares of Common Stock, for which I have enclosed in the amount of . Please register my stock certificate as follows:

Name(s): ______________________________

____

Address: ______________________________

Tax I.D. #: ______________________________

Very truly yours,

____

Name: ______________________________

Exhibit 10.6

CERULEAN PHARMA INC.

NONSTATUTORY STOCK OPTION AGREEMENT
GRANTED UNDER 2014 STOCK INCENTIVE PLAN

1. Grant of Option.

This agreement evidences the grant by Cerulean Pharma Inc., a Delaware corporation (the "Company"), on , 20 (the "Grant Date") to (the "Participant"), of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2014 Stock Incentive Plan (the "Plan"), a total of shares (the "Shares") of common stock, $0.0001 par value per share, of the Company ("Common Stock") at a price of $ per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on (the "Final Exercise Date").

It is intended that the option evidenced by this agreement shall not be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code"). Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("vest") as follows: .

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be in writing in the Form of Notice of Stock Option Exercise attached hereto, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or by such other method as shall be approved by the Company, in any case together with payment in full in the manner provided in the Plan. The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, officer or director of, or consultant or advisor (as such terms are defined and interpreted for purposes of Form S-8 under the Securities Act of 1933, as amended) to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an "Eligible Participant").

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon written notice to the Participant from the Company describing such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for "cause" as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment or other relationship with the Company is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment or other relationship. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment or other relationship by the Company for Cause, and the effective date of such employment or other termination is subsequent to the date of the delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's employment or other relationship shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment or other relationship (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate immediately upon the effective date of such termination of employment or other relationship). If the Participant is party to an employment, consulting or severance agreement with the Company that contains a definition of "cause" for termination of employment or other relationship, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant's employment or other relationship shall be considered to have been terminated for "Cause" if the Company determines, within 30 days after the Participant's resignation, that termination for Cause was warranted.

4. Withholding.

No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

5. Transfer Restrictions.

This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

6. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

[*Remainder of page intentionally left blank.*]

IN WITNESS WHEREOF, the Company has caused this option to be executed under its corporate seal by its duly authorized officer. This option shall take effect as a sealed instrument.

CERULEAN PHARMA INC.

By: ______________________________

Name: ______________________________

Title: ______________________________

PARTICIPANT'S ACCEPTANCE

The undersigned hereby accepts the foregoing option and agrees to the terms and conditions thereof. The undersigned hereby acknowledges receipt of a copy of the Company's 2014 Stock Incentive Plan.

PARTICIPANT:

____

Address: __________________________

____

FORM OF NOTICE OF STOCK OPTION EXERCISE

Date:

Cerulean Pharma Inc.
840 Memorial Drive
Cambridge, MA 02139

Attention: Treasurer

Dear Sir or Madam:

I am the holder of a Nonstatutory Stock Option granted to me under the Cerulean Pharma, Inc. (the "Company") 2014 Stock Incentive Plan (the "Plan") on for the purchase of shares of common stock, par value $0.0001 per share, of the Company ("Common Stock") at a purchase price of $ per share.

I hereby exercise my option with respect to shares of Common Stock for which I have enclosed in the amount of .

Please register my stock certificate as follows:

Name(s): ______________________________

____

Address: ______________________________

Tax I.D. #: ______________________________

Very truly yours,

____

Name: ______________________________

Exhibit 10.26

CERULEAN PHARMA INC.

2014 EMPLOYEE STOCK PURCHASE PLAN

, 2014

The purpose of this Plan is to provide eligible employees of Cerulean Pharma Inc. (the “Company”) and certain of its subsidiaries with opportunities to purchase shares of the Company’s common stock, $0.0001 par value (the “Common Stock”), commencing at such time as the Board of Directors of the Company (the “Board”) shall determine. Subject to adjustment under Section 15 hereof, the number of shares of Common Stock that have been approved for this purpose is the sum of:

(a) 500,000 shares of Common Stock; plus

(b) an annual increase to be added on the first day of each fiscal year, commencing on January 1, 2015 and ending on January 1, 2024, equal to the least of (i) 600,000 shares of Common Stock, (ii) 1% of the outstanding shares on such date, or (iii) an amount determined by the Board.

This Plan is intended to qualify as an “employee stock purchase plan” as defined in Section 423 of the Internal Revenue Code of 1986, as amended (the “Code”), and the regulations issued thereunder, and shall be interpreted consistent therewith.

1. Administration. The Plan will be administered by the Board or by a Committee appointed by the Board (the “Committee”). The Board or the Committee has authority to make rules and regulations for the administration of the Plan and its interpretation and decisions with regard thereto shall be final and conclusive.

2. Eligibility. All employees of the Company and all employees of any subsidiary of the Company (as defined in Section 424(f) of the Code) designated by the Board or the Committee from time to time (a “Designated Subsidiary”), are eligible to participate in any one or more of the offerings of Options (as defined in Section 9) to purchase Common Stock under the Plan provided that:

(a) they are customarily employed by the Company or a Designated Subsidiary for more than 20 hours a week and for more than five months in a calendar year;

(b) they have been employed by the Company or a Designated Subsidiary for at least 30 days prior to enrolling in the Plan; and

(c) they are employees of the Company or a Designated Subsidiary on the first day of the applicable Plan Period (as defined below).

No employee may be granted an Option hereunder if such employee, immediately after the Option is granted, owns 5% or more of the total combined voting power or value of the stock of the Company or any subsidiary. For purposes of the preceding sentence, the attribution rules of Section 424(d) of the Code shall apply in determining the stock ownership of an employee, and all stock that the employee has a contractual right to purchase shall be treated as stock owned by the employee.

The Company retains the discretion to determine which eligible employees may participate in an offering pursuant to and consistent with Treasury Regulation Sections 1.423-2(e) and (f).

3. Offerings. The Company will make one or more offerings (“Offerings”) to employees to purchase stock under this Plan. Offerings will begin at such time as the Board shall determine. Each Offering will consist of a six-month period (a “Plan Period”) during which payroll deductions will be made and held for the purchase of Common Stock at the end of the Plan Period. The Board or the Committee may, at its discretion, choose a different Plan Period of not more than twelve (12) months for Offerings.

4. Participation. An employee eligible on the first day of a Plan Period of any Offering may participate in such Offering by completing and forwarding either a written or electronic payroll deduction authorization form to the employee’s appropriate payroll office at least 15 days prior to the commencement of the applicable Plan Period. The form will authorize a regular payroll deduction from the Compensation received by the employee during the Plan Period. Unless an employee files a new form or withdraws from the Plan, his or her deductions and purchases will continue at the same rate for future Offerings under the Plan as long as the Plan remains in effect. The term “Compensation” means the amount of money reportable on the employee’s Federal Income Tax Withholding Statement, excluding overtime, shift premium, incentive or bonus awards, allowances and reimbursements for expenses such as relocation allowances for travel expenses, income or gains associated with the grant or vesting of restricted stock, income or gains on the exercise of Company stock options or stock appreciation rights, and similar items, whether or not shown or separately identified on the employee’s Federal Income Tax Withholding Statement, but including, in the case of salespersons, sales commissions to the extent determined by the Board or the Committee.

5. Deductions. The Company will maintain payroll deduction accounts for all participating employees. With respect to any Offering made under this Plan, an employee may authorize a payroll deduction in any percentage amount (in whole percentages) up to a maximum of 15% of the Compensation he or she receives during the Plan Period or such shorter period during which deductions from payroll are made. The Board or the Committee may, at its discretion, designate a lower maximum contribution rate. The minimum payroll deduction is such percentage of Compensation as may be established from time to time by the Board or the Committee.

6. Deduction Changes. An employee may decrease or discontinue his or her payroll deduction once during any Plan Period, by filing either a written or electronic new payroll deduction authorization form. However, an employee may not increase his or her payroll deduction during a Plan Period. If an employee elects to discontinue his or her payroll deductions during a Plan Period, but does not elect to withdraw his or her funds pursuant to Section 8 hereof, funds deducted prior to his or her election to discontinue will be applied to the purchase of Common Stock on the Exercise Date (as defined below).

7. Interest. Interest will not be paid on any employee accounts, except to the extent that the Board or the Committee, in its sole discretion, elects to credit employee accounts with interest at such rate as it may from time to time determine.

8. Withdrawal of Funds. An employee may at any time prior to the close of business on the fifteenth business day prior to the end of a Plan Period and for any reason permanently draw out the balance accumulated in the employee's account and thereby withdraw from participation in an Offering. Partial withdrawals are not permitted. The employee may not begin participation again during the remainder of the Plan Period during which the employee withdrew his or her balance. The employee may participate in any subsequent Offering in accordance with terms and conditions established by the Board or the Committee.

9. Purchase of Shares.

(a) Number of Shares. On the first day of each Plan Period, the Company will grant to each eligible employee who is then a participant in the Plan an option (an "Option") to purchase on the last business day of such Plan Period (the "Exercise Date") at the applicable purchase price (the "Option Price") up to that number of shares of Common Stock determined by multiplying $2,083 by the number of full months in the Plan Period and dividing the result by the closing price (as determined below) on the first day of such Plan Period; provided, however, that no employee may be granted an Option which permits his or her rights to purchase Common Stock under this Plan and any other employee stock purchase plan (as defined in Section 423(b) of the Code) of the Company and its subsidiaries, to accrue at a rate which exceeds $25,000 of the fair market value of such Common Stock (determined at the date such Option is granted) for each calendar year in which the Option is outstanding at any time; and, provided, further, however, that the Committee may, in its discretion, set a fixed maximum number of shares of Common Stock that each eligible employee may purchase per Plan Period which number may not be greater than the number of shares of Common Stock determined by using the formula in the first clause of this Section 9(a) and which number shall be subject to the second clause of this Section 9(a).

(b) Option Price. The Board or the Committee shall determine the Option Price for each Plan Period, including whether such Option Price shall be determined based on the lesser of the closing price of the Common Stock on (i) the first business day of the Plan Period or (ii) the Exercise Date, or shall be based solely on the closing price of the Common Stock on the Exercise Date; provided, however, that such Option Price shall be at least 85% of the applicable closing price. In the absence of a determination by the Board or the Committee, the Option Price will be 85% of the lesser of the closing price of the Common Stock on (i) the first business day of the Plan Period or (ii) the Exercise Date. The closing price shall be (a) the closing price (for the primary trading session) on any national securities exchange on which the Common Stock is listed or (b) the average of the closing bid and asked prices in the over-the-counter-market, whichever is applicable, as published in a source selected by the Board or the Committee. If no sales of Common Stock were made on such a day, the price of the Common Stock shall be the reported price for the next preceding day on which sales were made.

(c) Exercise of Option. Each employee who continues to be a participant in the Plan on the Exercise Date shall be deemed to have exercised his Option at the Option Price on such date and shall be deemed to have purchased from the Company the number of whole shares of Common Stock reserved for the purpose of the Plan that his accumulated payroll deductions on such date will pay for, but not in excess of the maximum numbers determined in the manner set forth above.

(d) Return of Unused Payroll Deductions. Any balance remaining in an employee’s payroll deduction account at the end of a Plan Period will be automatically refunded to the employee, except that any balance that is less than the purchase price of one share of Common Stock will be carried forward into the employee’s payroll deduction account for the following Offering, unless the employee elects not to participate in the following Offering under the Plan, in which case the balance in the employee’s account shall be refunded.

10. Issuance of Certificates. Certificates representing shares of Common Stock purchased under the Plan may be issued only in the name of the employee, in the name of the employee and another person of legal age as joint tenants with rights of survivorship, or (in the Company’s sole discretion) in the name of a brokerage firm, bank, or other nominee holder designated by the employee. The Company may, in its sole discretion and in compliance with applicable laws, authorize the use of book entry registration of shares in lieu of issuing stock certificates.

11. Rights on Retirement, Death or Termination of Employment. If a participating employee’s employment ends before the last business day of a Plan Period, no payroll deduction shall be taken from any pay then due and owing to the employee and the balance in the employee’s account shall be paid to the employee. In the event of the employee’s death before the last business day of a Plan Period, the Company shall, upon notification of such death, pay the balance of the employee’s account (a) to the executor or administrator of the employee’s estate or (b) if no such executor or administrator has been appointed to the knowledge of the Company, to such other person(s) as the Company may, in its discretion, designate. If, before the last business day of the Plan Period, the Designated Subsidiary by which an employee is employed ceases to be a subsidiary of the Company, or if the employee is transferred to a subsidiary of the Company that is not a Designated Subsidiary, the employee shall be deemed to have terminated employment for the purposes of this Plan.

12. Optionees Not Stockholders. Neither the granting of an Option to an employee nor the deductions from his or her pay shall make such employee a stockholder of the shares of Common Stock covered by an Option under this Plan until he or she has purchased and received such shares.

13. Options Not Transferable. Options under this Plan are not transferable by a participating employee other than by will or the laws of descent and distribution, and are exercisable during the employee’s lifetime only by the employee.

14. Application of Funds. All funds received or held by the Company under this Plan may be combined with other corporate funds and may be used for any corporate purpose.

15. Adjustment for Changes in Common Stock and Certain Other Events.

(a) Changes in Capitalization. In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under this Plan, (ii) the share limitations set forth in Section 9, and (iii) the Option Price shall each be equitably adjusted to the extent determined by the Board or the Committee.

(b) Reorganization Events.

(1) Definition. A "Reorganization Event" shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Options. In connection with a Reorganization Event, the Board or the Committee may take any one or more of the following actions as to outstanding Options on such terms as the Board or the Committee determines: (i) provide that Options shall be assumed, or substantially equivalent Options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) upon written notice to employees, provide that all outstanding Options will be terminated immediately prior to the consummation of such Reorganization Event and that all such outstanding Options will become exercisable to the extent of accumulated payroll deductions as of a date specified by the Board or the Committee in such notice, which date shall not be less than ten (10) days preceding the effective date of the Reorganization Event, (iii) upon written notice to employees, provide that all outstanding Options will be cancelled as of a date prior to the effective date of the Reorganization Event and that all accumulated payroll deductions will be returned to participating employees on such date, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the "Acquisition Price"), change the last day of the Plan Period to be the date of the consummation of the Reorganization Event and make or provide for a cash payment to each employee equal to (A) (1) the Acquisition Price times (2) the number of shares of Common Stock that the employee's accumulated payroll deductions as of immediately prior to the Reorganization Event could purchase at the Option Price, where the Acquisition Price is treated as the fair market value of the Common Stock on the last day of the applicable Plan Period for purposes of determining the Option Price under Section 9(b) hereof, and where the number of shares that could be purchased is subject to the limitations set forth in Section 9(a), minus (B) the result of multiplying such number of shares by such Option Price, (v) provide that, in connection with a liquidation or dissolution of the Company, Options shall convert into the right to receive liquidation proceeds (net of the Option Price thereof) and (vi) any combination of the foregoing.

For purposes of clause (i) above, an Option shall be considered assumed if, following consummation of the Reorganization Event, the Option confers the right to purchase, for each share of Common Stock subject to the Option immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common

Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); provided, however, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise of Options to consist solely of such number of shares of common stock of the acquiring or succeeding corporation (or an affiliate thereof) that the Board determines to be equivalent in value (as of the date of such determination or another date specified by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

16. Amendment of the Plan. The Board may at any time, and from time to time, amend or suspend this Plan or any portion thereof, except that (a) if the approval of any such amendment by the shareholders of the Company is required by Section 423 of the Code, such amendment shall not be effected without such approval, and (b) in no event may any amendment be made that would cause the Plan to fail to comply with Section 423 of the Code.

17. Insufficient Shares. If the total number of shares of Common Stock specified in elections to be purchased under any Offering plus the number of shares purchased under previous Offerings under this Plan exceeds the maximum number of shares issuable under this Plan, the Board or the Committee will allot the shares then available on a pro-rata basis.

18. Termination of the Plan. This Plan may be terminated at any time by the Board. Upon termination of this Plan all amounts in the accounts of participating employees shall be promptly refunded.

19. Governmental Regulations. The Company’s obligation to sell and deliver Common Stock under this Plan is subject to listing on a national stock exchange (to the extent the Common Stock is then so listed or quoted) and the approval of all governmental authorities required in connection with the authorization, issuance or sale of such stock.

20. Governing Law. The Plan shall be governed by Delaware law except to the extent that such law is preempted by federal law.

21. Issuance of Shares. Shares may be issued upon exercise of an Option from authorized but unissued Common Stock, from shares held in the treasury of the Company, or from any other proper source.

22. Notification upon Sale of Shares. Each employee agrees, by entering the Plan, to promptly give the Company notice of any disposition of shares purchased under the Plan where such disposition occurs within two years after the date of grant of the Option pursuant to which such shares were purchased.

23. Grants to Employees in Foreign Jurisdictions. The Company may, to comply with the laws of a foreign jurisdiction, grant Options to employees of the Company or a Designated Subsidiary who are citizens or residents of such foreign jurisdiction (without regard to whether they are also citizens of the United States or resident aliens (within the meaning of

Section 7701(b)(1)(A) of the Code)) with terms that are less favorable (but not more favorable) than the terms of Options granted under the Plan to employees of the Company or a Designated Subsidiary who are resident in the United States. Notwithstanding the preceding provisions of this Plan, employees of the Company or a Designated Subsidiary who are citizens or residents of a foreign jurisdiction (without regard to whether they are also citizens of the United States or resident aliens (within the meaning of Section 7701(b)(1)(A) of the Code)) may be excluded from eligibility under the Plan if (a) the grant of an Option under the Plan to a citizen or resident of the foreign jurisdiction is prohibited under the laws of such jurisdiction or (b) compliance with the laws of the foreign jurisdiction would cause the Plan to violate the requirements of Section 423 of the Code. The Company may add one or more appendices to this Plan describing the operation of the Plan in those foreign jurisdictions in which employees are excluded from participation or granted less favorable Options.

24. Authorization of Sub-Plans. The Board may from time to time establish one or more sub-plans under the Plan with respect to one or more Designated Subsidiaries, provided that such sub-plan complies with Section 423 of the Code.

25. Withholding. If applicable tax laws impose a tax withholding obligation, each affected employee shall, no later than the date of the event creating the tax liability, make provision satisfactory to the Board for payment of any taxes required by law to be withheld in connection with any transaction related to Options granted to or shares acquired by such employee pursuant to the Plan. The Company may, to the extent permitted by law, deduct any such taxes from any payment of any kind otherwise due to an employee.

26. Effective Date and Approval of Shareholders. The Plan shall become effective upon the closing of our initial public offering.

Adopted by the Board of Directors on
March 25, 2014

Approved by the stockholders on
March 26, 2014

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the use in this Amendment No. 2 to Registration Statement No. 333-194442 of our report dated March 7, 2014 (March 31, 2014 as to the effects of the reverse stock split described in Note 18), relating to the financial statements of Cerulean Pharma Inc. (which report expresses an unqualified opinion and includes an explanatory paragraph relating to the Company's ability to continue as a going concern) appearing in the Prospectus, which is a part of such Registration Statement, and to the reference to us under the heading "Experts" in such Prospectus.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 31, 2014