UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2014

Or

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

For the transition period from to

Commission File No. 001-36395

Cerulean Pharma Inc.

(Exact name of registrant as specified in its charter)

Delaware	**20-4139823**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
840 Memorial Drive Cambridge, MA	**02139**
(Address of principal executive offices)	**(Zip Code)**

617-551-9600

(Registrant's telephone number, including area code)

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

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	**The NASDAQ Global Market**

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

None

(Title of Class)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (Section 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2014 was approximately $74,209,799.40, based on the closing price of the registrant's common stock on The NASDAQ Global Market.

As of March 16, 2015, there were 20,375,987 of the Registrant's common shares, $0.0001 par value, issued and outstanding.

PART I

Cautionary Note on Forward Looking Statements

Any statements in this Annual Report on Form 10-K about our future expectations, plans and prospects, including statements about the clinical development of our product candidates, statements about our estimated research and development expenses and sufficiency of cash to fund specified use of cash and other statements containing the words "anticipate," "believe," "continue," "could," "estimate," "expect," "hypothesize," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the uncertainties inherent in the initiation of clinical trials, availability and timing of data from ongoing and future clinical trials and the results of such trials, whether preliminary results from a clinical trial will be predictive of the final results of that trial or whether results of early clinical trials will be indicative of the results of later clinical trials, expectations for regulatory approvals, availability of funding sufficient for our foreseeable and unforeseeable operating expenses and capital expenditure requirements and other factors discussed in Item 1A of this Annual Report on Form 10-K under the heading "Risk Factors". In addition, any forward-looking statements included in this Form 10-K represent our views only as of the date hereof and should not be relied upon as representing our views as of any subsequent date. We specifically disclaim any obligation to update any forward-looking statements.

Item 1. Business

Overview

We are a clinical-stage, oncology-focused company applying our proprietary Dynamic Tumor Targeting™ Platform to develop differentiated therapies. We were incorporated under the laws of the State of Delaware on November 28, 2005 under the name Tempo Pharmaceuticals, Inc. In October 2008, we changed our name to Cerulean Pharma Inc. Our platform utilizes nanoparticle-drug conjugates, or NDCs, which consist of proprietary polymers that are covalently linked to anti-cancer therapeutics, or payloads. We believe these NDCs 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. We believe that our NDCs are differentiated from other nanoparticle technologies by our linker technology, which allows for preferential delivery of our anti-cancer payloads.

Our lead product candidate, CRLX101, is a dynamically tumor targeted NDC in Phase 2 clinical development and has the potential to improve outcomes for patients in combination with other cancer treatments. 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. Two products that have been marketed by other companies, irinotecan and topotecan, inhibit topo 1, but their utility is limited by toxicities. Recent research suggests that HIF, and in particular the HIF subunit HIF-la, is a master regulator of multiple cancer cell survival pathways. Over 250 patients have been administered CRLX101 in multiple indications at several clinical trial sites. In clinical trials evaluating CRLX101 as a single agent, CRLX101 was generally well tolerated with a toxicity profile generally characterized by low-grade (Common Terminology Criteria for Adverse Events grade 1-2) adverse events. No treatment-related trial deaths have been observed to date. In ongoing clinical trials, CRLX101 also appears active and combinable with Avastin (bevacizumab) and chemoradiotherapy, or CRT, which is a combination of capecitabine and radiation. In addition, preclinical data indicate that CRLX101 may be combinable with other anti-cancer therapies. We are pursuing development of CRLX101 in combination with anti-cancer therapies in multiple ongoing clinical development programs that include a company-sponsored trial and investigator-sponsored trials, or ISTs. These trials consist of:

- *Relapsed renal cell carcinoma:*
    - A Phase 2 randomized, controlled, company-sponsored trial is being conducted comparing CRLX101 administered in combination with Avastin to investigator's choice of standard of care in patients with renal cell carcinoma, or RCC, who have received two or three prior lines of therapy. We refer to this study as the RCC Trial. The RCC Trial is currently being conducted at approximately 30 sites in the United States, with eight additional sites planned in the United States and five additional sites planned in South Korea. Based on results from the Phase 1b/2 IST in relapsed RCC, discussed below, we believe that the combination of CRLX101 and Avastin may provide therapeutic benefits to patients with RCC who have received two or three prior lines of therapy including a tyrosine kinase inhibitor, or TKI, and/or an inhibitor of a mammalian target of rapamycin, or an mTORI.

- A Phase 1b/2 single-arm IST of CRLX101 in combination with Avastin in patients with relapsed RCC is being conducted at the University of Pennsylvania and Thomas Jefferson University Hospital. A total of 22 patients were enrolled in this trial. The last patient was enrolled in December 2014, and the trial has met its primary endpoint of at least 50% of patients achieving four months progression free survival, or PFS. Preliminary data from this clinical trial has been submitted for presentation at the 2015 annual meeting of the American Society of Clinical Oncology, or ASCO. As of February 3, 2015, the date of the abstract submission to ASCO, the median PFS, or mPFS, of patients on trial was 9.9 months, with seven of the 22 patients still receiving treatment. Based on third-party published data, the mPFS of the standard of care in this setting is approximately 3.5 months. In addition, the Response Evaluation Criteria in Solid Tumor, or RECIST, partial response rate of patients on the trial as of February 3, 2015 was 23%. Several recent studies in advanced RCC suggest that after treatment with a TKI, subsequent therapies, including Avastin alone, achieve RECIST partial response rates of between 2% and 4%.

- *Relapsed ovarian cancer:*

  - A Phase 2 single-arm IST of CRLX101 as monotherapy and in combination with Avastin in patients with relapsed ovarian cancer is being conducted at Massachusetts General Hospital and affiliated Harvard University teaching hospitals. As previously reported, the first stage of the trial, administering CRLX101 as monotherapy, met its primary endpoint of PFS at six months for at least four patients. RECIST responses, as well as encouraging PFS, were observed for several patients. Platinum-resistant ovarian cancer patients are being enrolled in the second stage of this trial, administering CRLX101 in combination with Avastin.

  - We have commenced start-up activities for a Phase 1b single-arm company-sponsored trial of CRLX101 in combination with weekly paclitaxel in patients with relapsed ovarian cancer conducted in collaboration with the GOG Foundation, Inc. (formerly known as the Gynecologic Oncology Group), or GOG.

- *Neoadjuvant rectal cancer:*

  - A Phase 1b/2 single-arm IST of CRLX101 in combination with CRT in patients with non-metastatic rectal cancer is being conducted at the University of North Carolina at Chapel Hill and several other sites, including the University of Indiana, Wake Forest University, Rex Hospital Inc. and Southeastern Medical Oncology Center. No dose limiting toxicities, or DLTs, have been reported in the Phase 1b stage of the trial, in which a maximum tolerated dose, or MTD, and recommended Phase 2 dose, or RP2D, of 15 mg/m2 of CRLX101 was established when administered in combination with capecitabine and radiotherapy. Patients are currently being enrolled in the RP2D expansion Phase 2 stage of the trial.

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 ability of NDCs to target the "leaky" vasculature that is present in all solid tumors 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 other cancer therapies. Our development focus is on tumor types where HIF is up-regulated, topo 1 inhibition is desirable, and drug combinations with CRLX101 can be pursued.

CRLX301, our second platform-generated clinical candidate, is a dynamically tumor-targeted NDC in Phase 1 clinical development. CRLX301 is designed to concentrate in tumors and slowly release its anti-cancer payload, docetaxel, inside tumor cells. Docetaxel is a microtubule stabilizer that is extensively used in clinical practice and is approved by the FDA for the treatment of locally advanced or metastatic non-small cell lung cancer, locally advanced squamous cell carcinoma of the head and neck, androgen-independent prostate cancer, locally advanced or metastatic breast cancer and advanced gastric cancer. In preclinical studies, CRLX301 delivered up to ten times more docetaxel into tumors, compared to an equivalent milligram dose of commercially available docetaxel and was superior to docetaxel in seven of seven animal models, with a statistically significant survival benefit seen in five of the seven models. In addition, preclinical data show that CRLX301 had lower toxicity than has been reported with docetaxel in similar preclinical studies. 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.

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 NDCs for the treatment of patients with inadequately treated forms of cancer. Key elements of our strategy to achieve this goal are to:

- *Advance the clinical development of our lead product candidate, CRLX101, in multiple tumor types.* Based on confirmatory signals of activity observed in the ongoing relapsed RCC IST, we initiated a randomized Phase 2 clinical trial of CRLX101 in combination with Avastin in this patient population in 2014. We are exploring development opportunities in two additional tumor types, and we intend to explore additional development opportunities, alone and in collaboration with strategic partners, to capitalize on the various opportunities to use CRLX101 in combination with other cancer treatments.

- *Advance the clinical development of our second product candidate, CRLX301, into selected indications.* Assuming we are successful in establishing a safe maximum tolerated dose, or MTD, and/or a recommended Phase 2 dose in the Phase 1 trial, we plan to rapidly advance CRLX301 into Phase 2 development.

- *Leverage our platform to discover and develop a proprietary pipeline of highly differentiated product candidates with anti-cancer payloads*. Using our Dynamic Tumor Targeting Platform, we have created two product candidates, CRLX101 and CRLX301. We have used our platform to create additional NDCs, 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 payloads. 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 active pharmaceutical ingredients, or APIs, that can be used as NDC payloads for use in the treatment of 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 NDCs 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.

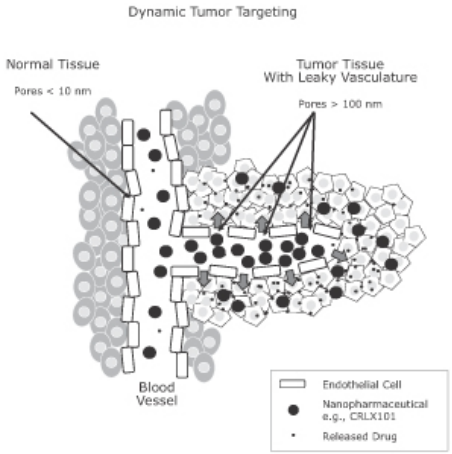
Our Approach to Developing Dynamically Tumor Targeted NDCs

Our Dynamic Tumor Targeting Platform is designed to create NDCs with the aim of providing safer and/or more effective therapies for patients living with cancer. This platform has thus far generated a lead candidate, CRLX101, and a second candidate, CRLX301, and has the potential to expand our pipeline, alone and in combination with partners.

Our proprietary Dynamic Tumor Targeting Platform utilizes cyclodextrin polymer, or CDP, technology, which we use to create NDCs that contain small molecules such as camptothecin in the case of CRLX101 and docetaxel in the case of CRLX301. NDCs 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, we believe 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 NDCs are generally 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 a separate 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 NDC and sustained release of the NDC'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 NDCs circulate in the bloodstream. In contrast to typical small molecule drugs, once in the bloodstream, our NDCs are generally 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. 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. 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 NDCs are typically between 10 and 40 nanometers in diameter.

   CRLX101 has a relatively low tissue distribution. A compound's volume of distribution refers to the theoretical 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 irinotecan, an analog of camptothecin approved for the treatment of metastatic colon cancer, is approximately 263 liters, and the volume of distribution of topotecan, which is approved for the treatment of ovarian, cervical and small cell lung cancer, is approximately 130 liters. This low tissue distribution of CRLX101 spares key organ systems from extensive drug exposure.

   Our NDCs are designed to be stealthy, meaning that they are designed to be not readily detected by the body's immune cells and therefore avoid producing an immune response. This results in slow metabolism and long systemic circulation, allowing our NDCs 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 NDCs into the interior of tumor cells. We believe that macropinocytosis acts as the primary 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 NDC and its anti-cancer payload. Following their entry into the cancer cells, we believe our NDCs, due to their size, are not easily removed from cancer cells by their existing 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 NDC, 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 NDC 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 plasma drug concentration to reach half of its original value, of two to three hours in humans, whereas CRLX101 has a plasma 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 NDCs 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.

As initial clinical evidence of selective entry of CRLX101 in tumor tissue, we obtained differential post-therapy biopsies of tumor tissue and adjacent normal tissue from two gastric patients. 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 observed safety profile of our lead drug candidate, CRLX101, across more than 250 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 a range of API 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 NDCs 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, a relatively high potency of the payload, as well as intellectual property, regulatory and commercial considerations. As discussed below, in preclinical testing, our NDCs generally show improved pharmacokinetics, activity and tolerability as compared to the payload alone. We intend to develop NDCs alone and potentially in collaboration with partners.

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 NDCs 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 began clinical development of CRLX301 in 2014.

Product Candidate	Indication	Stage	Design of Ongoing Clinical Trials
CRLX101	Relapsed Renal Cell Carcinoma	Phase 2	•Ongoing randomized Phase 2 company-sponsored trial of CRLX101 in combination with Avastin •Ongoing single-arm Phase 1b/2 IST of CRLX101 in combination with Avastin that has completed enrollment
	Relapsed Ovarian Cancer	Phase 2	•Ongoing 2-part, single-arm Phase 2 IST of CRLX101 as monotherapy and in combination with Avastin o Part 1: monotherapy arm that met primary efficacy and safety endpoints o Part 2: ongoing single-arm of CRLX101 in combination with Avastin, for which the Avastin is provided by Genentech
	Neoadjuvant Rectal Cancer	Phase 2	•Ongoing single-arm Phase 1b/2 IST of CRLX101 in combination with CRT
CRLX301	Solid Tumors	Phase 1	•Ongoing Phase 1 dose-escalation trial of CRLX301 as monotherapy

CRLX101

CRLX101 is a dynamically tumor targeted NDC that is administered intravenously. It includes a CDP 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 important 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, will lead to differentiated efficacy. Initially, we are focusing on combinations with vascular endothelial growth factor inhibitors, or VEGF inhibitors, or CRT. Accordingly, we are currently developing CRLX101 in combination with Avastin in relapsed RCC and relapsed ovarian cancer, and in combination with CRT in rectal cancer in the neoadjuvant setting.

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 tissue distribution and toxicity related to camptothecin. Our hypothesis is that this delivery mechanism results in the release of the active form of camptothecin into the tumor cells, allowing it to 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

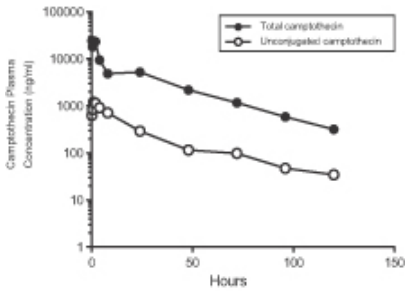
cells replicate and transcribe their DNA more frequently than normal cells, they require frequent re-ligation of broken DNA strands and are more sensitive to topo 1 inhibitors than normal cells.

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.

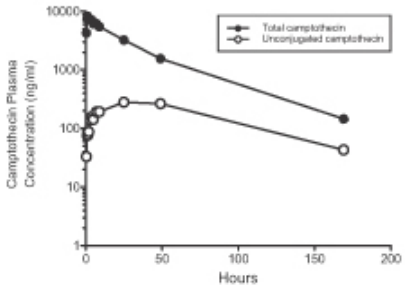
We conducted a preclinical study in which rats were dosed with 2.59 mg/kg of CRLX101, and the concentrations of camptothecin, total and unconjugated, meaning after its release from CRLX101, were measured using liquid chromatography/tandem mass spectrometry. As illustrated in the graph below, plasma concentration 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 37 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 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



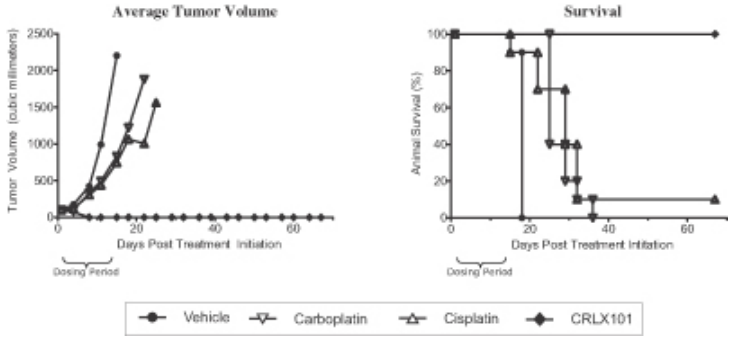
The results from this pharmacokinetic rat study, demonstrating long half-life, slow clearance and low volume of distribution, were consistent with the results of our Phase 1/2a clinical trial of CRLX101 in advanced multiply pre-treated solid tumor malignancies, in which human patients were dosed with 15 mg/m2 of CRLX101 which is the single agent maximum tolerated dose. In the Phase 2a trial, blood was drawn from 36 patients after their first dose of CRLX101 and analyzed for total and unconjugated camptothecin using liquid chromatography/tandem mass spectrometry. The half-life of conjugated camptothecin 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, RCC, 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.

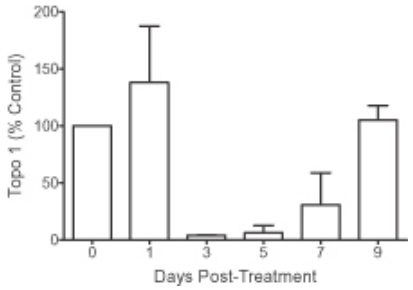
The following graphs illustrate the tumor volume results and post-treatment survival rates in a preclinical study comparing CRLX101 to Paraplatin® (carboplatin) and cisplatin, which are platinum-based chemotherapeutic agents, in an ovarian xenograft model. In this study, we treated nude mouse xenograft 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 MTD 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 subcutaneous and orthotopic xenograft models, which is a model in which a tumor is grafted into the animal in its natural location, encompassing RCC, ovarian cancer, head and neck cancer, and triple negative breast cancer, demonstrated additive or synergistic effect, meaning greater than additive 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.

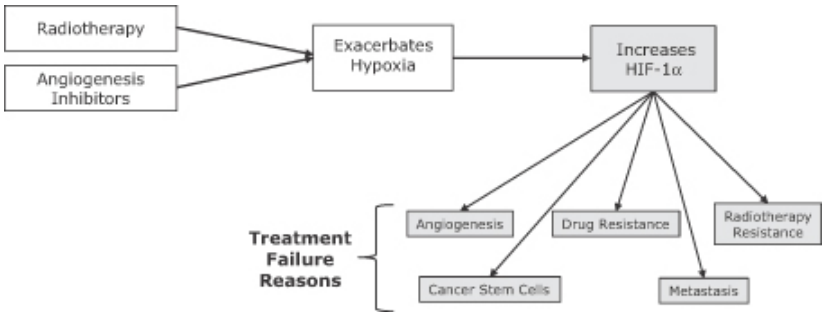
Topo 1 Protein in Tumors After CRXL101 Treatment



In addition to inhibiting topo 1, CRLX101 is a potent, durable and combinable inhibitor of HIF-1α and HIF-2α protein expression. The compounds in the camptothecin compound family, including camptothecin and topotecan, have been described as inhibitors of HIF-1α in the past. However, the literature suggests that to achieve durable inhibition of HIF-1α, sustained concentrations of camptothecin or topotecan must be achieved within tumor cells. Due to its short half-life, low tumor targeting and high toxicities, topotecan cannot effectively achieve durable HIF-1α inhibition unless it is dosed metronomically (continuous or frequent treatment with low doses of anti-cancer drugs), which is not considered to be clinically feasible given its toxicity profile.

HIF-1α 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-1α is a master regulator for several key 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-1α slows down, thus leading to a buildup of HIF-1α. According to the Nature Reviews Clinical Oncology paper, independent researchers demonstrated that the buildup of HIF-1α 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 chemo and radiotherapy resistance and cancer metastasis. While anti-angiogenesis drugs can achieve impressive tumor shrinkage and PFS 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-1α 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 schematic 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-1a 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 hypothesize that the simultaneous inhibition of topo 1 and HIF-1a by CRLX101 will lead to significant clinical benefit, particularly if combined with anti-cancer therapies that are known to create hypoxia and up-regulate HIF-1a.

In addition to showing that CRLX101 inhibits HIF-1a in preclinical tumor models, we have further demonstrated that the NDC 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. Finally, we have also observed the synergy of CRLX101 with other VEGF inhibitors such as Votrient and Zaltrap.

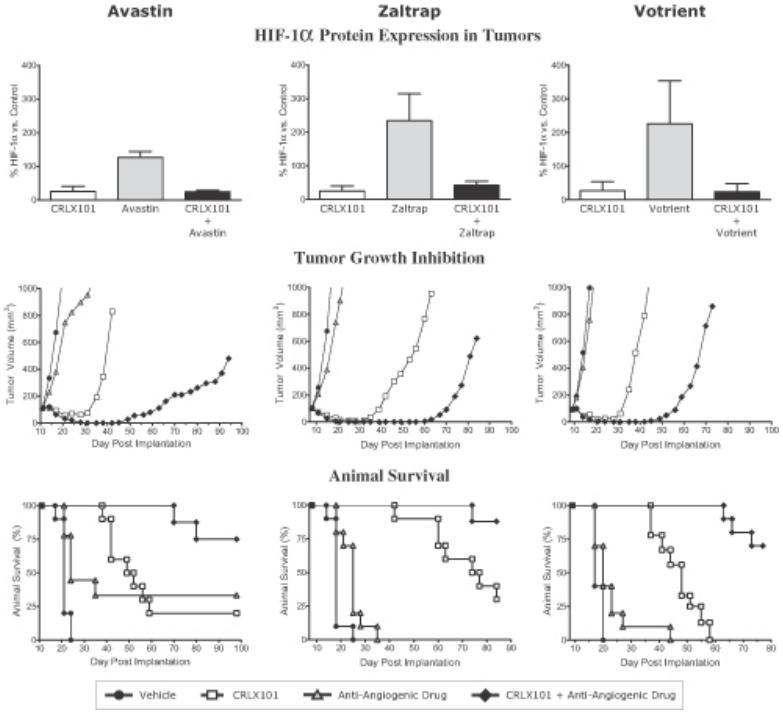
We have conducted animal tumor model studies comparing CRLX101 to certain leading anti-angiogenesis drugs and the combination of CRLX101 and these anti-angiogenesis drugs. In these studies, we treated nude mouse xenograft models in which human A2780 ovarian cancer tumor cells were implanted subcutaneously 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-1α protein expression was significantly up-regulated in the presence of each tested anti-angiogenesis drug;
- HIF-1α 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-1α protein expression was down-regulated compared to control, thus confirming that the CRLX101 down-regulation can counteract the HIF-1α 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.



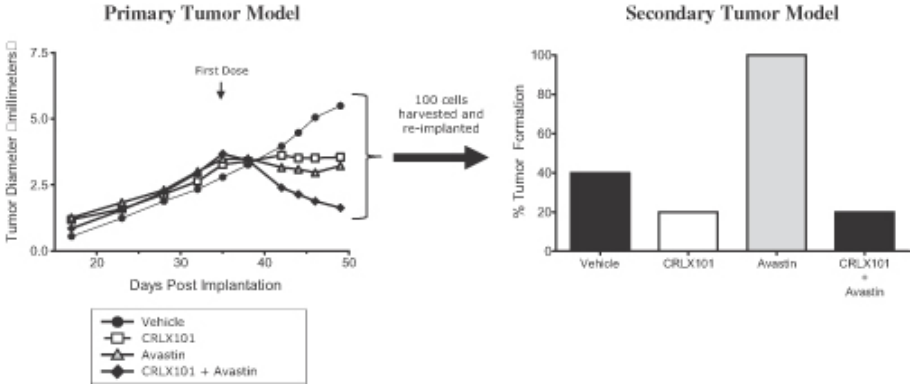
We have achieved similar results in a preclinical study of the effect on cancer stem cells of exposure to CRLX101 alone and CRLX101 in combination with Avastin. In this study, we treated nude mouse xenograft models in which human SUM159 triple-negative breast cancer tumor cells were implanted orthotopically 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.

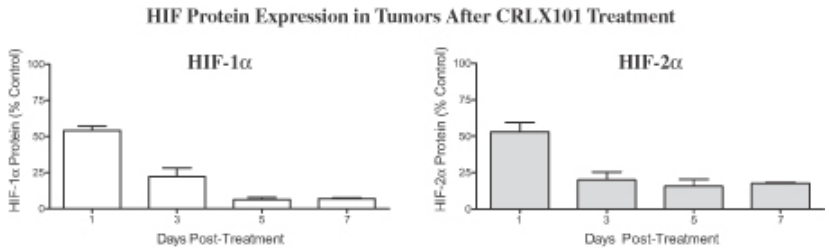
In these cancer stem cell functional experiments:

- 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-1α CRLX101 also appears to durably inhibit HIF-2α. 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-1α and HIF-2α 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-1α by over 90%, and reduced HIF-2α 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.



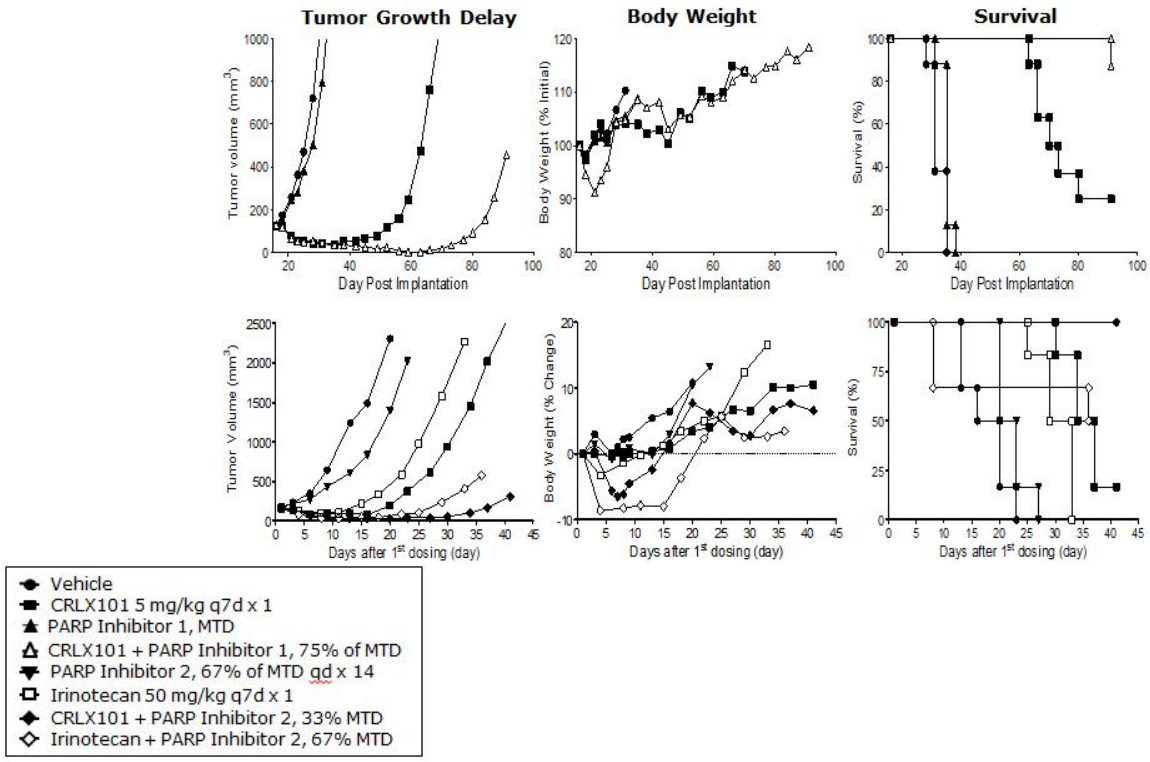
Radiotherapy is frequently used for the treatment of solid tumor malignancies that have not extensively metastasized and are accessible, and thus a radiation beam can be deployed with the goal of destroying the tumor. For example, rectal cancer and head and neck cancers are often treated with radiotherapy. 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. It is well documented that topo 1 inhibitors can enhance the effects of radiotherapy, i.e. act 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 enhance the effects of radiation, (2) a HIF-1a inhibitor to prevent the radiotherapy-induced up-regulation of HIF-1a and its associated induced resistance to radiotherapy, (3) a tumor targeted agent that focuses the radiosensitization in the tumors, (4) an agent with a favorable safety profile to allow the combination with radiotherapy and (5) 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 animal tumor models of head and neck cancer and colorectal 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.

We believe there are other possible combinations for CRLX101, including with Poly ADP ribose polymerase inhibitors, or PARP inhibitors. PARP inhibitors hinder a cell's ability to repair single-strand DNA breaks. Topo 1 inhibitors, such as camptothecin and its analogs, create persistent single-strand DNA breaks, and preclinical experiments have shown that PARP inhibition potentiates the DNA damage resulting from topo 1 inhibition. Results from preclinical studies have established the combined activity of topo 1 inhibition and PARP inhibition, however, clinical trials of this combination approach, including clinical trials of veliparib plus topotecan and Lynparza® (olaparib) plus topotecan in solid tumors, resulted in significant toxicities that necessitated dose reductions, which in turn resulted in sub-therapeutic dose levels for both drugs and limited clinical development progress. CRLX101 has been shown to be generally well-tolerated as monotherapy and appears to be a combinable topo-1 inhibitor at its MTD. The observed safety profile of CLRX101, along with clinical experience combining CRLX101 (at its MTD) with other agents, supports our hypothesis that CRLX101 may facilitate PARP inhibitor and topo 1 inhibitor combinations that are not possible with the currently approved topo 1 inhibitors.

The graphs below show data from mouse experiments we conducted in which CRLX101 was combined with each of two different PARP inhibitors. In the study with the first PARP inhibitor, nude mouse xenograft models were implanted subcutaneously with human NCI-H1048 small cell lung cancer tumor cells and allowed to establish tumors. The mice were divided into three dose groups, with each dose group consisting of three animals. We administered one intravenous dose of 5 mg/kg of CRLX101 to the first dose group, ten daily oral doses of the PARP inhibitor at its MTD to the second dose group, and one dose of 5 mg/kg of CRLX101 in combination with 10 daily doses of the PARP inhibitor 1 at 75% of its MTD to the third dose group. The graphs in the top row reflect the results of the combination of CRLX101 and the first PARP inhibitor in the mice. As illustrated in these graphs, treatment with CLRX101 and the PARP inhibitor resulted in a mean bodyweight loss in the mice of approximately 10% that was recoverable. In addition, the mice in this experiment experienced tumor growth delay and survival rates that were superior to the tumor growth delay and survival rates experienced by the mice that received placebo, CRLX101 or the PARP inhibitor alone.

In the study with the second PARP inhibitor, nude mouse xenograft models in two separate experiments were implanted subcutaneously with human NCI-H1048 small cell lung cancer tumor cells and allowed to establish tumors. In one experiment, the mice were divided into three dose groups, with each dose group consisting of six animals. Mice in the first dose group were administered one intravenous dose of 5 mg/kg CRLX101, mice in the second dose group were administered ten daily oral doses of the second PARP inhibitor at 66% of the MTD and mice in the third dose group were administered one dose of 5 mg/kg CRLX101 in combination with ten daily doses of the PARP inhibitor 2 at 33% of its MTD. In the second experiment, the mice were divided into three dose groups, with each dose group consisting of six animals. Mice in the first dose group were administered one intravenous dose of 50 mg/kg irinotecan, mice in the second dose group were administered ten daily oral doses of the second PARP inhibitor at 66% of its MTD, and mice in the third dose group were administered one dose of 50 mg/kg irinotecan in combination with ten daily doses of the PARP inhibitor at 66% of its MTD. The three graphs in the bottom row reflect the results of CRLX101 and the second PARP inhibitor in the mice and also show the results of the same PARP inhibitor and irinotecan in a separate experiment. As illustrated in these graphs, the mice dosed with the MTD of CRLX101 and 33% of the MTD of the second PARP inhibitor experienced tumor regression after a single dose, and the mean tumor volume did not return to its size at the onset of dosing until day 33 of the study. In contrast, mice dosed with 66% of the MTD of this second PARP inhibitor together with a sub-MTD dose of irinotecan did not achieve the same extent of tumor growth inhibition, and two of the six mice died during treatment.



Note: Irinotecan and PARP Inhibitor 2 experiments were not performed at the same time as CRLX101 and PARP Inhibitor 2 experiments.

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 chemoradiotherapy or VEGF inhibitors that increase levels of HIF; and
- 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 RCC in combination with Avastin, relapsed ovarian cancer in combination with Avastin and neoadjuvant rectal cancer in combination with CRT.

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 an MTD of 15mg/m2 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 myelosuppression, 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 MTD in the Phase 1 portion of the clinical trial, an additional 38 patients were enrolled in a Phase 2a MTD 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, (as described below) 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 MTD of 15mg/m2. Mean elimination unconjugated Tmax 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, MTD 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, or mPFS, for patients treated in the Phase 1/2a trial at the MTD was 3.7 months. The best response per RECIST criteria was stable disease in 28 patients, or 64%, treated at the MTD, 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/m2 weekly dosing prior to discontinuing for progressive disease, or PD. In a subset of 22 patients with NSCLC, mPFS 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, mPFS, 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 PFS and overall survival comparable to

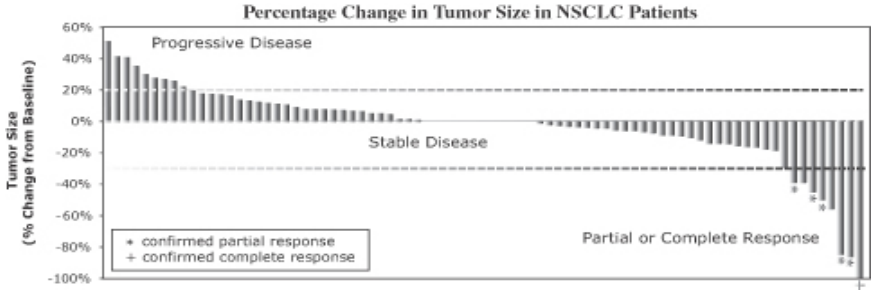
the PFS and overall survival observed in approved cancer therapies in this setting. Disease progression and tumor response rates were determined in accordance with RECIST criteria.

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.

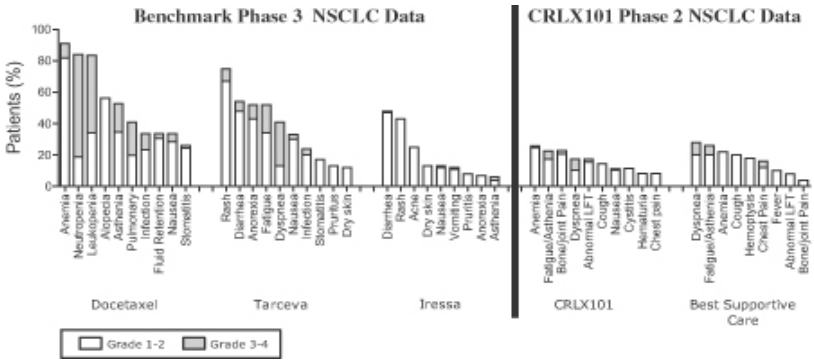
We believe these imbalances in withdrawal rates and post-trial cancer treatment between the CRLX101 and best supportive care arms caused an upward skewing of the median overall survival of the best supportive care population. This belief is supported by benchmark data on median overall survival in previous 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 computed tomography, or 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.

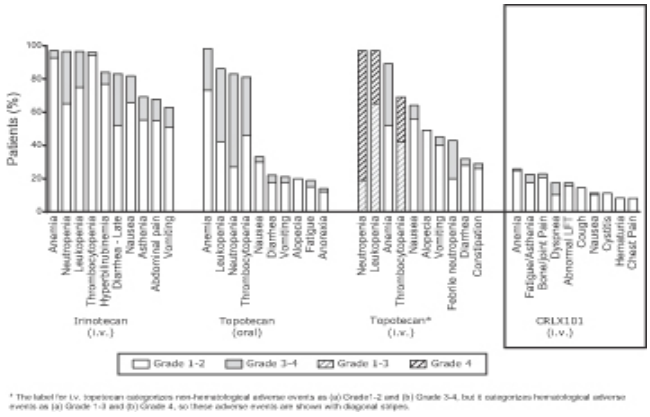


The adverse events experienced in the CRLX101 arm of the clinical trial were generally low grade and manageable. They were similar to the adverse events experienced on the best supportive care arm of the trial, and they were relatively less severe than the adverse events experienced in clinical trials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



Potential for Combinability

A drug eligible for combination therapy should demonstrate a safety profile that does not overlap with or exacerbate the safety profile of the combination agent. The visual depiction below represents the adverse events experienced by patients in the CRLX101 arm of the NSCLC trial and the adverse events experienced by patients in clinical trials of approved camptothecin-class therapeutics, irinotecan and topotecan. As CRLX101 was generally well tolerated in the NSCLC trial, we believe this early 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 estimates that 62,000 new cases of kidney cancer will occur in the United States in 2015 and that approximately 14,000 people will die from kidney cancer in 2015. According to the most recently available data from Surveillance, Epidemiology, and End Results Program of the United States National Cancer Institute, the incidence of kidney cancer has been generally rising each year. RCC is by far the most common type of kidney cancer, accounting for nine out of every ten kidney cases. Up to 30% of patients with RCC present with metastatic disease and five-year survival among these patients is less than 10%. There is currently no cure for RCC that has metastasized beyond the lymph nodes to one or more distant organs, which we refer to as metastatic RCC. There is currently no treatment specifically approved for the treatment of RCC in patients who have progressed on two or more prior lines of therapy. This unmet need creates an opportunity for a new class of therapies in this indication.

Systemic therapeutic options for advanced stage RCC 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 RCC have only modestly extended the median overall survival of patients.

While there are currently six FDA-approved therapies commonly used for the treatment of RCC, 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 PFS advantage of Inlyta® (axitinib) over Nexavar® (sorafenib) in the second-line treatment of advanced RCC. 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 PFS 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 RCC.

Rationale for Use of CRLX101 for Relapsed RCC: A variety of renal epithelial cell types can transform into RCC. Clear cell RCC comprises approximately 85% of renal cell carcinomas. The most commonly identified genetic aberrations in clear cell tumors are those resulting in loss of the von Hippel Lindau tumor suppressor gene. This loss in turn leads to higher intracellular levels of HIF-1α and HIF-2α, 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-1α and HIF-2α 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 PFS and response rate benefits achieved with Avastin in this setting into meaningful overall survival benefits for RCC patients.

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

We are currently enrolling a Phase 2 randomized company-sponsored trial of CRLX101 in combination with Avastin in relapsed RCC. This trial is currently being conducted in approximately 30 cancer centers in the United States, with eight additional sites planned in the United States and five additional sites planned in South Korea, and is designed to enroll 110 patients with unresectable metastatic RCC who have completed 2 or 3 prior regimens of therapy. The primary endpoint of this trial will compare PFS among 90 clear cell RCC patients treated with concurrently administered CRLX101 and Avastin versus an investigator's choice of standard of care agent not previously used in the same patient. Statistical power is set at 80% to detect a 2.3 month improvement in mPFS over an expected 3.5 months in the comparator arm. Secondary and exploratory endpoints include overall survival, response rate, safety, pharmacokinetics, and plasma biomarkers of efficacy. Additionally, 20 patients with non-clear cell RCC histologies will be evaluated independently.

Laying the foundation for this randomized trial, a single arm Phase 1b/2 IST of CRLX101 in combination with Avastin was conducted and has now completed enrollment at the University of Pennsylvania and Thomas Jefferson University Hospital. Relapsed RCC patients with metastatic or locally advanced disease who were previously treated with at least one prior molecularly targeted therapy, such as a TKI or mTORI, were eligible to participate. Two dose-levels of CRLX101, 12 mg/m2 and 15 mg/m2, delivered intravenously once every two weeks, were evaluated in combination with standard Avastin dosing of 10 mg/kg delivered intravenously once every two weeks. This clinical trial employed 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 MTD of CRLX101 administered in combination with Avastin. CT-based tumor evaluations occurred every two cycles. The primary endpoint of the Phase 1b stage was to identify the MTD of CRLX101 in combination with Avastin in this indication, and the primary endpoint of the Phase 2 stage was PFS at four months. Secondary objectives include objective response rate and assessment of toxicity.

The last patient was enrolled in this Phase 1b/2 IST in December 2014, and the trial has met its primary endpoint of at least 50% of patients achieving four months PFS. Preliminary data from this clinical trial has been submitted for presentation at the 2015 annual meeting of the American Society of Clinical Oncology, or ASCO. As of February 3, 2015, the date of the abstract submission to ASCO, the mPFS of patients on the trial was 9.9 months, with seven of the 22 patients still receiving treatment. Based on third-party published data, the mPFS of the standard of care in this setting is approximately 3.5 months. In addition, the RECIST partial response rate of patients on the trial as of February 3, 2015 was 23%. Several recent studies in advanced RCC suggest that after treatment with a TKI, subsequent therapies, including Avastin alone, achieve RECIST partial response rates of between 2% and 4%. CRLX101 in combination with Avastin was generally well tolerated in this trial. Full data for all 22 patients has been submitted for presentation at the 2015 annual meeting of ASCO.

Our planned initial indication for CRLX101 in the treatment of RCC is in combination with Avastin in patients who have progressed to a third or fourth line treatment regimen.

Relapsed Ovarian Cancer

Current Treatments for Ovarian Cancer: The American Cancer Society estimates that approximately 21,000 women in the United States will receive a new diagnosis of ovarian cancer in 2015 and that approximately 14,000 women in the United States will die from ovarian cancer in 2015, 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 was not approved for use in ovarian cancer until November 2014. Some patients will be primary refractory, meaning they will 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 was not FDA approved for this indication until November 2014 when it was approved in combination with any one of three chemo therapies based on data from the AURELIA trial, which is described below. 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 an international Phase 3 randomized clinical trial, which is referred to as the AURELIA trial, for the treatment of patients with second and third line platinum-resistant ovarian cancer conducted by Genentech, Inc. indicated that the addition of Avastin to chemotherapy provided notable response rates and PFS and a trend toward improvements in overall survival in particular patient sub-groups. Although the AURELIA trial did not achieve a statistically significant improvement in overall survival among all patients, it was the basis for FDA approval of Avastin in combination with any one of three chemotherapies in November 2014. Based on the AURELIA data and other trials evaluating the use of Avastin in ovarian cancer, it appears that benefits of VEGF inhibitors such as Avastin are suggested in this setting. We hypothesize that HIF-1α contributes to resistance to VEGF inhibitors, including Avastin. Furthermore, a comprehensive analysis of over-represented genes in ovarian cancer identifies HIF-1α as a highly active pathway common to both basal breast and serous ovarian cancers and suggests that HIF-1α may be an important therapeutic target in ovarian cancer. As highlighted above, CRLX101 appears to durably suppress HIF-1α 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, facilitated through the inhibition of HIF-1α, will potentiate the translation of PFS 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 preliminary clinical evaluation of this combination appears to be generally well tolerated thus far.

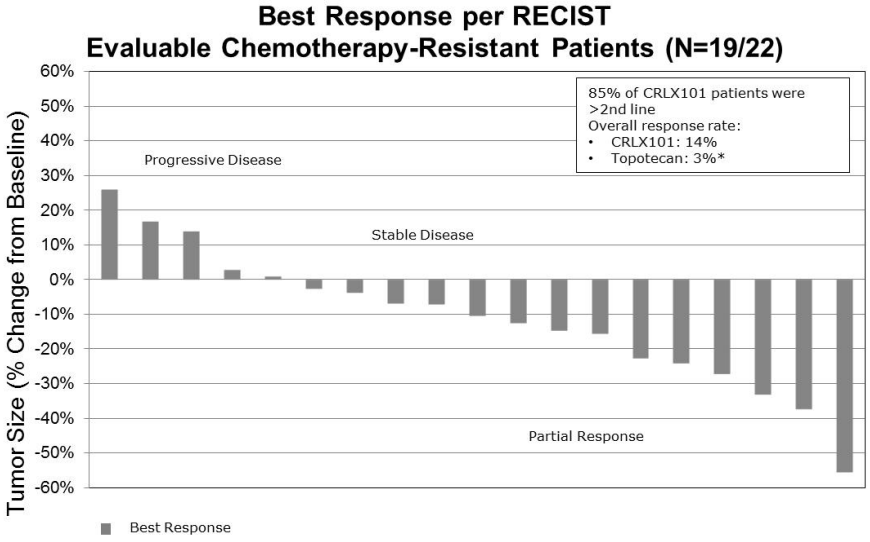
We also believe that CRLX101 could provide benefit to patients with relapsed ovarian cancer in combination with other cancer treatments, including paclitaxel. Weekly dosing of paclitaxel demonstrates both cytotoxic and anti-angiogenic activity in ovarian cancer and clinical trials have demonstrated both PFS and overall survival benefits of weekly paclitaxel dosing in this setting, even among patients with prior progression through dose-dense paclitaxel. Therefore, we hypothesize that CRLX101's potential to overcome HIF-related chemotherapy resistance is relevant to weekly paclitaxel and this combination has demonstrated greater than additive activity in pre-clinical models. We have commenced start-up activities for a company sponsored Phase 1b clinical trial, conducted in collaboration with GOG, evaluating CRLX101 in combination with weekly paclitaxel in relapsed ovarian cancer.

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 was conducted at Massachusetts General Hospital and affiliated Harvard teaching hospitals in Boston, Massachusetts. The primary endpoint of this trial was to achieve PFS at six months for at least four patients.

The primary PFS endpoint was met with seven patients having achieved PFS of six months or longer. In addition, 15 patients achieved net tumor shrinkages, with four patients having achieved RECIST-based partial responses. In addition, two patients remained active on trial for more than one year. 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. Of the 19 evaluable platinum-resistant patients, 18 demonstrated scan results showing stable disease or better for their target lesions, 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. 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 ongoing single arm Phase 2 clinical trial of CRLX101 dosed at 15mg/m2 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. The primary endpoint of the trial is PFS 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.

Our planned initial indication for CRLX101 in the treatment of ovarian cancer is not yet determined. We intend to use data from the ongoing IST in combination with Avastin and data from the planned trial in combination with weekly paclitaxel to help us determine the optimal approach to developing CRLX101 in ovarian cancer.

Neoadjuvant Rectal Cancer

Current Treatments for Neoadjuvant Rectal Cancer: The American Cancer Society estimates that approximately 39,600 people in the United States will be newly diagnosed with rectal cancer in 2015. Patients without distant metastases are candidates for neoadjuvant therapy, which consists of approximately six weeks of CRT. The goal of CRT 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, or pCR, is observed in approximately 10% to 20% of patients. A pCR following neoadjuvant chemoradiotherapy is associated with excellent long-term survival versus patients who do not achieve pCR (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.

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. Since it is well documented that topo 1 inhibitors can enhance the effects of radiotherapy, we expect CRLX101 to be an effective and well-tolerated radiosensitizer. In fact, combinations of irinotecan plus capecitabine or 5-FU plus radiotherapy have demonstrated pCR rates between 21% and 37% across various trials, which is greater than the pCR rates that have been demonstrated across various trials using capecitabine 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 and in combination with CRT in a colorectal 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-1α up-regulation in causing resistance to radiotherapy. Accordingly, we believe that CRLX101, with its durable topo 1 and HIF-1α inhibition, as well as its favorable safety profile, offers strong potential as an add-on drug to standard of care CRT 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 capecitabine and radiotherapy in patients with non-metastatic rectal cancer is being conducted at the University of North Carolina at Chapel Hill and other sites, including the University of Indiana, Wake Forest University, Rex Hospital Inc. and Southeastern Medical Oncology Center. This clinical trial is designed to identify the MTD of CRLX101 administered in combination with capecitabine and radiotherapy and to detect signals of increased clinical benefit over capecitabine and radiotherapy alone. The trial is designed to enroll up to 53 patients and has a primary endpoint of pCR rate as well as secondary endpoints of disease free survival and overall survival.

The MTD and recommended Phase 2 dose were established in the Phase 1b stage of the trial. The trial has therefore progressed to the Phase 2 stage. If we see pCR rates in excess of 30% for a limited number of patients in the IST, we expect to transition into a randomized Phase 2 trial of approximately 80 to 120 patients. This randomized trial would compare the safety and efficacy of CRLX101 plus CRT to CRT alone.

Assuming supportive data, we intend to transition into the Phase 2 randomized clinical trial. We also expect to engage with the FDA prior to the initiation of a Phase 2 randomized clinical trial to understand whether the agency agrees that pCR is an appropriate surrogate endpoint for use in connection with treatment of patients in the neoadjuvant setting as the basis for accelerated approval.

Our planned initial indication for CRLX101 in the treatment of rectal cancer is in combination with CRT in patients being treated in the neoadjuvant setting.

Other ISTs

Gastric Cancer. A single-arm Phase 2 pharmacodynamic clinical trial of CRLX101 in advanced HER 2 negative gastric cancer patients was conducted in an IST at the City of Hope National Comprehensive Cancer Center in Duarte, California. The trial objectives were to utilize tumor biopsies to establish differential NDC penetration between tumor and adjacent normal tissue and to establish signals of activity in HER-2 negative gastric cancer patients. Biopsies have been analyzed for differential drug accumulation between tumor and normal tissue using immunoflourescence techniques. Data from 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 these CRLX101 data in human cancer patients validate 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, was conducted in an IST at the University of Chicago and at other major medical centers in the United States. The trial objectives were to establish feasibility of enrolling this advanced patient population and to differentiate the safety and efficacy of CRLX101 at 15mg/m2 dosed every two weeks versus topotecan, the only approved second line SCLC agent. We expect this trial to close due to slow enrollment sometime in the second quarter of 2015.

Additional CRLX101 Development Opportunities

There are several factors that may allow combinations of CRLX101 with anti-cancer therapies beyond Avastin and CRT. This may include combinations with other chemotherapeutics, targeted chemotherapeutics, molecularly targeted agents and nanoparticles, 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-1α assays across multiple tumor models have shown CRLX101 to be a durable inhibitor of HIF-1α and to provide synergistic HIF-1α 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 platinum-based agents. 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 that repairs single strand DNA breaks. A combined inhibition of PARP and topo 1 has been shown to be a well-established cooperative interaction in preclinical research because PARP inhibitors prevent repair to single strand DNA breaks caused by topo 1 inhibitors. To date, the clinical potential of this combination has remained unrealized, as Phase 1 trials of PARP inhibitors with topotecan conducted by others have shown toxicities necessitating dose reductions to sub-therapeutic levels, limiting the ability to readily progress in further clinical development. We believe that, due to its potential for improved tolerability as compared to approved topo 1 inhibitors, CRLX101 may be combinable with PARP inhibitors at therapeutically active doses. The FDA recently approved the first PARP inhibitor, AstraZeneca's Lynparza, as monotherapy in patients with deleterious or suspected deleterious germline BRCA mutated (as detected by an FDA-approved test) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.

CRLX301

Overview

CRLX301 is an NDC with docetaxel as its anti-cancer payload. Docetaxel, a member of the taxane family, 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 locally advanced or metastatic NSCLC, locally advanced squamous cell carcinoma of the head and neck, androgen-independent prostate cancer, locally advanced or metastatic breast cancer and advanced gastric cancer. 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.

Because CRLX301 is synthesized in a similar manner as CRLX101, we can utilize some common 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 250 patients without serious toxicities attributed to the nanopharmaceutical backbone.

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

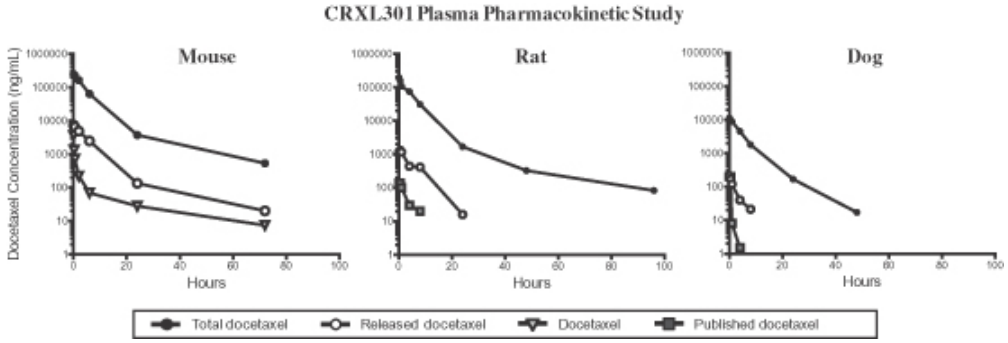
We believe that enhanced therapeutic benefit and a favorable safety profile for CRLX301 would enable combination therapies incorporating CRLX301 with other anti-cancer therapies that may not be combinable today due to docetaxel's toxicities.

CRLX301 Preclinical and IND-Enabling Data

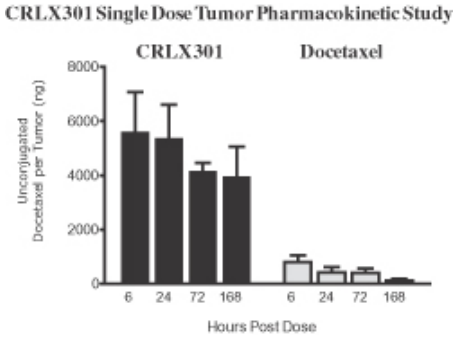
We have conducted the following PK studies in mice, rats and dogs in which CRLX301 demonstrated prolonged circulation as compared to docetaxel:

- 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.



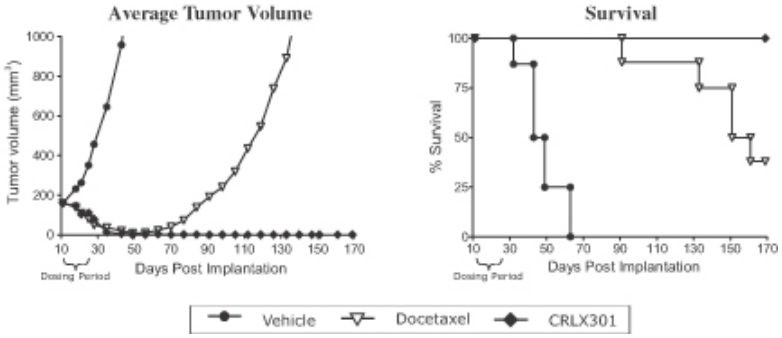
We have also measured tumor levels of CRLX301 that were approximately ten-times the tumor levels of docetaxel in a mouse tumor PK study. We measured concentrations of docetaxel in mice following administration of a single dose of either CRLX301 or docetaxel in mice, in which certain mouse melanoma tumor 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 four 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 five of these seven animal xenograft models (in each case, $p<.05$).

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 MTD for CRLX301 was approximately 20% higher compared to published data of the MTD for docetaxel in dogs. We observed no evidence of platform-based toxicities. The higher MTD 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 tissue distribution 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 to focus on the utility of this NDC to provide effective delivery of docetaxel into tumors for prolonged periods of time with reduced tissue distribution, enhancing anti-tumor activity while potentially reducing the toxicity observed with traditional taxanes. We commenced the Phase 1 portion of a Phase 1/2a clinical trial at two cancer centers in Australia in December 2014. This clinical trial allows first-in-human dosing of CRLX301 in patients with advanced solid tumor malignancies in order to evaluate the safety of the drug and establish an MTD. Patients in this Phase 1 portion of the clinical trial 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 are performed using RECIST guidelines, and patients are considered evaluable for efficacy if at least one dose of study drug is received.

Phase 1 patients are being enrolled, initially in single patient cohorts, and starting with the third cohort, in the 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 MTD 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.

We began Phase 1 clinical testing in Australia, and we submitted an IND to the FDA in February 2015, which will allow us to include additional cancer centers in the United States to the clinical trial. The Phase 2a portion of the trial is expected to enroll an additional 24 to 30 patients so that CRLX301 can be evaluated at the recommended Phase 2 dose established in the Phase 1 portion of

the trial in 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, ovarian cancer, cervical cancer, breast cancer, gastric cancer, prostate cancer, melanoma and head and neck cancer. In addition, once we have established a MTD, 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.

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 Agios Pharmaceuticals, Inc., ARIAD 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., TESARO, Inc. and Verastem, Inc.

Several companies are developing and marketing 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 squamous and KRAS mutated NSCLC), Celator Pharmaceuticals, Inc. (CPX-351 for acute myeloid leukemia), Celsion Corporation (ThermoDox (lyso-thermosensitive liposomal doxorubicin) for liver cancer and breast cancer), Cytimmune Sciences, Inc. (CYT-6091 for NSCLC) and Supratek Pharma Inc. (SP1049C for solid tumors). In addition, at least two companies have oncology product candidates in clinical development that are irinotecan reformulations: Merrimack Pharmaceuticals' liposomal irinotecan (MM-398 for pancreatic and colorectal cancer) and Nektar Therapeutics' etirinotecan pegol (NKTR-102 for breast cancer).

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

In relapsed RCC, the six FDA-approved therapies commonly used for treatment represent only two mechanistic classes—VEGF inhibitors and mTORIs—and there are no approved cytotoxic drugs. Antibodies against PD-1/PD-L1 are in late stage development in relapsed RCC. Exelixis' TKI, cabozantinib, TRACON Pharmaceuticals, Inc.'s TRC105, and Acceleron Pharma, Inc.'s dalantercept (the latter two are in combination with axitinib) are in development in second line or later stage relapsed RCC. Regardless of the results of these trials, we believe that there will remain a place for VEGF targeted therapies, and therefore a role for CRLX101, if approved, in treating patients who progress on a VEGF targeted agent. In relapsed ovarian cancer, there are multiple approved therapies, including most recently Avastin, in combination with chemotherapy, and Lynparza, and multiple companies developing therapeutic candidates in various stages of development. For example, OncoMed Pharmaceuticals is developing demcizumab, and Genentech, Inc. 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, capecitabine, which is marketed by Genentech, Inc., was approved for use in rectal cancer in 2005. Capecitabine 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 capecitabine. There are also several development programs for the treatment of rectal cancer in the neoadjuvant setting. Isofol Medical is developing a molecule that is currently labeled to [6R] 5,10-methylenetetrahydrofolate, Karyopharm Therapeutics, Inc. is developing Selinexor in combination with chemoradiation, Merck KgAA is developing Tecemotide with chemoradiotherapy, Genentech, Inc. is testing Avastin in combination with capecitabine, and Kadmon is developing KD018 in combination with capecitabine and radiation. Immunomedics, Inc. has IMMU-130, an anti-CEACAM5 antibody conjugated to SN-38, a topo 1 inhibiting drug. This program is currently in Phase 2 trials in metastatic colorectal cancer.

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 in squamous and KRAS NSCLC. 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 CTI BioPharma's paclitaxel poliglumex, in late stage clinical development as maintenance therapy for advanced ovarian cancer.

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, in some cases through an assignment from Calando, or exclusively license from Caltech, 16 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 19 issued United States patents and 31 issued foreign counterparts, as well as over 22 pending United States patent applications and over 54 pending foreign applications. These patents and applications, if issued, generally will expire between 2018 and 2035. 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

- Seven 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 or CDP conjugates administered in combination with another agent (United States patents and foreign counterparts would, if issued, expire between 2030 and 2035). One of these seven 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, 13 patent families which generally relate to nanoparticles containing selected polymers linked to a therapeutic agent or another molecule. These patent families include 18 United States patent applications and 36 foreign applications and one issued foreign patent. These patent applications, if issued, generally will expire between 2025 and 2035. 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;

- Four 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 2035). 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 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, China, the European Union, India, 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 and China. 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 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 symbol ™ indicates a common law trademark. Other service marks, trademarks and trade names appearing elsewhere in this Annual Report on Form 10-K 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 CRLX101 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 CRLX101 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. Upon the initiation of our CRLX301 Phase 1 trial in 2014, we made a milestone payment of $250,000 to Calando. 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 five times, including to extend or suspend the time period for achieving certain diligence milestones, and the most recent amendment was entered into in February 2015. 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 June 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 September 2015, MIT will have the right, in its sole discretion, to terminate the agreement. If, prior to the end of September 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, 2014, 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.

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, 2014, 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 through 2015, and have begun manufacturing additional supplies to continue clinical development of CRLX101 beyond 2015. 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 and cGMP Phase 1 clinical supply.

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 RCC, 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 of the clinical trial(s) by an independent institutional review board(s), or IRB(s), representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trial(s) 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 summarizing available data to support the proposed approval of the new drug product for the proposed use;
- review of the product by an FDA advisory committee, as may be requested by the FDA to assist with its review;
- satisfactory completion of FDA inspection(s) 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 (per published PDUFA guidelines for that year) 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.

Nonclinical Studies

Nonclinical 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. They also include in vitro and animal studies to assess the safety and activity of the drug to start dose assessment for initial testing in humans and to further 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 for clinical investigation in the U.S. 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 IND and 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, major amendments 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: Phase 1 includes the initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal volunteer subjects. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the toxicities associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies. The total number of subjects and patients included in Phase 1 studies varies with the drug, but are generally smaller than later stage studies. Phase 1 studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.

Phase 2: Phase 2 includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase 2 studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects.

Phase 3: Phase 3 studies are expanded trials, generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase 3 studies usually include from several hundred to several thousand subjects.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA through the IND 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

In order to protect the rights and welfare of human research subjects and to verify the quality and integrity of data submitted to the FDA in support of marketing applications, the FDA monitors all aspects of FDA-regulated research through a comprehensive program of on-site inspections and data audits. Under the Agency's Bioresearch Monitoring Program, FDA field investigators and headquarters' scientists conduct site visits of research sponsors, clinical investigators, contract research organizations, IRBs, radioactive drug research committees, and non-clinical (animal) laboratories.

In general, the FDA accepts foreign safety and efficacy studies that were not conducted under an IND provided that they are well designed, well conducted, performed by qualified investigators, and conducted in accordance with ethical principles acceptable to the world community. The conduct of these studies must meet at least minimum standards for assuring human subject protection. Therefore, for studies submitted in support of an NDA that were conducted outside the U.S. and not under an IND, the agency requires demonstration that such studies were conducted in accordance with Good Clinical Practices.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply:

- Patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;

- The potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context of the disease or condition to be treated; and
- The expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

FDA regulations allow access to investigational drugs under an IND by the company or the treating physician (see investigator-sponsored trials below) for treatment purposes on a case-by-case basis for:

- individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings);
- intermediate-size patient populations (groups of patients, n >1); and
- larger populations for use of the drug under a treatment protocol or Treatment IND Application.

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 investigational (unapproved) indication 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, the company, 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, the IRB, 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.

Submission of an NDA to the FDA

Detailed information and results from preclinical and clinical studies and other requirements relating to the product's chemistry, manufacture, controls and proposed labeling 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 $2.3 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $110,000 per product and $569,000 per establishment for fiscal year 2015. These fees are typically increased annually. Important exceptions or waivers for user fees include:

- A small company (fewer than 500 employees, including employees and affiliates) may submit a written request for a waiver by the FDA to waive the application fee for its first human drug application. After a waiver for a first human drug application is granted, the small business is assessed appropriate user fees for all subsequent human drug applications and supplements submitted for review.
- Products with Orphan Drug Designation for a particular indication are not subject to an application user fee provided there are no other intended uses in the NDA.

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. "Standard review", representing most such applications is generally reviewed within ten months from the date of filing. "Priority review", as may be designated by the FDA for a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness, are targeted to be reviewed within six months from the date 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 meeting specific criteria to assure compliance with GCP. The FDA may also inspect the company to evaluate, for example, processes, safety reporting procedures, training and compliance with US regulations as the sponsor.

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, intended to expedite drug development, and priority review designation, intended to expedite review and approval of an NDA.

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 regarding drug development and the company may submit sections of a fast track product's NDA before the application is complete. A rolling review must be communicated to and agreed upon by the FDA. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information. The sponsor must pay the applicable user fee upon submission of the first module in the rolling submission. However, the FDA's time period goal for reviewing a rolling NDA does not begin until the last module of the NDA is submitted. Notably, 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.

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. The FDA may take certain actions with respect to breakthrough therapies, including holding increased 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. In oncology, new products with breakthrough therapy designation have occasionally been approved well before the PDUFA review timeline, even for priority review, has elapsed.

An NDA for a drug will receive priority review designation by the FDA 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.

Accelerated approval will be subject to the requirement that the applicant study the drug further, to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome. Post-marketing studies would usually be studies already underway. When required to be conducted, such studies must also be adequate and well-controlled. The applicant shall carry out any such studies with due diligence.

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 additional, sometimes substantial, 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 or without 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.

Section 505(b)(2) NDAs

FDA approval of most new drug products is based on applications containing two full clinical trials that 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, if the investigations made to show whether the drug is safe and effective and relied upon by the applicant were not conducted by or for the applicant and the applicant has not obtained a right of reference from the person by or for whom the investigations were conducted. If the 505(b)(2) applicant can establish that reliance on the FDA's previous finding of safety and efficacy is appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the proposed new product.

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.

The Best Pharmaceuticals for Children Act (BPCA) is intended to improve the FDA and applicant accountability for the agreed-upon pediatric studies by creating a new mechanism for funding pediatric studies that sponsors or holders of approved applications declined to conduct voluntarily. Pediatric exclusivity, 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 that 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.

In some oncology indications, where pediatric studies are impossible or highly impractical (because, for example, the number of pediatric patients is so small or geographically dispersed), it may be possible to request a waiver.

Orphan Drug 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.

Pharmaceutical companies developing an orphan drug to treat an uncommon disease may be eligible for the research tax credit for qualified research expenses or the orphan drug tax credit for development costs attributable to qualified clinical testing incurred in developing the drug.

Unless otherwise required by regulation, the pediatric data requirements under the Pediatric Research Equity Act do not apply to products with orphan designation.

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, using the appropriate registration 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. The working definition includes all malignant and borderline malignant neoplasms, following the current International Classification of Diseases for Oncology, including primary or secondary malignant neoplasms, carcinoma in situ, and neoplasms classified as uncertain whether benign or malignant. Medicinal products for cancer treatment include antineoplastic agents (including modulators and enhancers of antineoplastic activity) and adjuvant treatments. 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.

The Committee for Medicinal Products for Human Use, or CHMP, is responsible for preparing EMA's opinions on all questions concerning medicines for human use, in accordance with European regulation. In the centralized procedure, the CHMP is responsible for conducting the initial assessment of medicines for which an EU-wide marketing authorization is sought. 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 CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization.

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, 2015, we had 39 full-time employees, including a total of 13 employees with M.D. or Ph.D. degrees. Of our workforce, 15 employees are engaged in research and development. None of our employees is represented by labor unions or covered by collective bargaining agreements.

Item 1A. Risk Factors

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

Risks Related to Our Financial Position and Need for Additional Capital

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

We expect our expenses to increase in connection with our ongoing activities, particularly as we advance the clinical development of CRLX101 and CRLX301 and continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other future product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. In particular, the costs that may be required for the manufacture of any product candidate that receives marketing approval may be substantial, and manufacturing our nanoparticle-drug conjugates, or NDCs, for commercial sale will require expensive and specialized facilities, processes and materials. Furthermore, relative to previous years when we operated as a private company, we expect to incur significant additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding 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 our current cash and cash equivalents to fund our ongoing research and development efforts. We will be required to expend significant funds in order to advance development of CRLX101, CRLX301 and our other potential product candidates. Our existing cash and cash equivalents will not be sufficient to fund all of the efforts that we plan to undertake, such as additional randomized trials of CRLX101 or CRLX301. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations or licensing arrangements or other sources. Adequate and additional funding may not be available to us on acceptable terms or at all.

On January 8, 2015, we entered into a loan and security agreement, which we refer to as the Hercules Loan Agreement, with Hercules Technology Growth Capital, Inc., or Hercules, and drew the first tranche of $15.0 million under the Hercules Loan Agreement. Although the Hercules Loan Agreement provides for two additional tranches in an aggregate amount of up to $11.0 million that we may borrow if we meet certain clinical and financing milestones, we may fail to meet these conditions and be unable to obtain this funding.

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

We believe that our cash and cash equivalents as of December 31, 2014, plus the $15.0 in proceeds we borrowed from Hercules under the first tranche of the Hercules Loan Agreement and the $1.0 million in proceeds we received from the sale of our common stock to Hercules in a private placement transaction that was completed in connection with the Hercules Loan Agreement, will enable us to fund our operating expenses, debt service and capital expenditure requirements into the third quarter of 2016. 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.

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

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

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

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

As of December 31, 2014, we had $3.3 million of outstanding indebtedness under our loan and security agreement with Lighthouse Capital Partners VI, L.P., or Lighthouse Capital. On January 8, 2015, we entered into the Hercules Loan Agreement and drew the first tranche of $15.0 million. We used $3.6 million of the proceeds from our draw under the Hercules Loan Agreement to repay in full our outstanding indebtedness under our loan and security agreement with Lighthouse Capital. As of February 28, 2015, we had approximately $15.1 million in outstanding indebtedness under the Hercules Loan Agreement.

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

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, and prepayment and repayment fees and penalties, thereby reducing money available to fund working capital, capital expenditures, product development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;

- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

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

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

Since incorporation, we have incurred significant operating losses. As of December 31, 2014, we had an accumulated deficit of $121.8 million. We do not know whether or when we will become profitable. We have not generated any revenues to date from product sales and have financed our operations primarily through the public offering of our common stock, private placements of our preferred stock, convertible debt financings and secured debt financings. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- initiate and continue company-sponsored clinical trials of CRLX101, our most advanced product candidate, including single-arm trials and randomized trials;
- support ongoing and any new investigator-sponsored clinical trials, or ISTs, of CRLX101;
- continue our 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;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- in the future, establish a sales, marketing and distribution infrastructure in the United States 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; and
- hire additional personnel.

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

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the United States Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, to perform

studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

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

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

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

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

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

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

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

We are focused on applying our proprietary Dynamic Tumor Targeting Platform to develop drugs that address serious unmet medical needs. We believe that our Dynamic Tumor Targeting Platform has the potential to create drugs that may have significant utility in several cancer indications, particularly in combination with other cancer 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 NDCs, which are a new way of targeting tumors. The regulatory review process for novel product candidates, such as ours, can be more expensive and take longer than for product candidates based on more well-known or extensively studied technologies due to regulatory authorities' lack of experience with them. As a result, we may be required to conduct additional studies and/or trials beyond those we anticipate and it may take us longer to develop and/or obtain regulatory approval for our existing and any future product candidates than we expect.

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

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of CRLX101 for the treatment of patients with inadequately treated forms of cancer. Our prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize CRLX101. The success of CRLX101 will depend, among other things, on our ability to successfully complete clinical trials of CRLX101. The clinical trial process is uncertain, and failure of one or more clinical trials can occur at any stage of testing. For example, in 2011, we initiated an

open-label, randomized Phase 2 clinical trial of CRLX101 as monotherapy in patients with advanced NSCLC who had progressed through one or two prior regimens of chemotherapy. In this Phase 2 clinical trial, CRLX101 failed to meet its primary endpoint of improvement in overall survival of the CRLX101-treated group as compared to the control arm of the study, which was best supportive care.

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

- receipt of marketing approvals from the FDA or other applicable regulatory authorities;
- the performance of our future collaborators for CRLX101, if any;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment 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.

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

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

- the size and nature of the patient population;
- the severity of the disease under investigation;
- unexpected or serious adverse events that occur in the trials;
- the proximity of patients to sites;
- the eligibility criteria for the trial;
- the design of the trial;
- efforts to facilitate timely enrollment;
- investigators' engagement with, or enthusiasm about, the trial;
- complexity of initiating or expanding trials with sites outside of the United States;

- competing trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

For example, with respect to our company-sponsored trial of CRLX101 in combination with Avastin (bevacizumab) in patients with 3rd and 4th line relapsed renal cell carcinoma, or the RCC Trial, which we initiated in August 2014, site accrual was slower than expected, so we are adding additional sites with the goal of completing enrollment according to plan; however, we may not be able to achieve this goal.

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 are currently pursuing the clinical development of CRLX101 in combinations with Avastin in relapsed renal cell carcinoma and relapsed ovarian cancer and with capecitabine 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, capecitabine, 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 renal cell carcinoma, or RCC, that has relapsed, (2) in combination with Avastin in patients with relapsed ovarian cancer and (3) in combination with capecitabine and radiotherapy in patients with neoadjuvant rectal cancer. We have also commenced the RCC Trial, which is a company-sponsored trial, and we expect to commence additional company-sponsored trials of CRLX101 in the future. Avastin is currently approved to treat various cancers, and the combination of capecitabine 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 capecitabine. 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 capecitabine, we will not be able to market CRLX101 in combination with such revoked therapeutic. If safety or efficacy issues arise with Avastin or capecitabine 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. Moreover, if Avastin or capecitabine were to receive regulatory approval in combination with a different therapeutic in any indication for which we are pursuing approval, such approval could impact the feasibility and design of any subsequent clinical trials that we may seek to conduct evaluating CRLX101 in combination with Avastin or capecitabine, as applicable. If capecitabine 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 CRLX101 prior to any regulatory approval in this indication. In addition, if manufacturing, cost or other issues result in a supply shortage of Avastin, capecitabine 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 capecitabine or another therapeutic, we would continue to be subject to the risk that the FDA could revoke its approval of Avastin or capecitabine, that safety, efficacy, manufacturing, cost or supply issues could arise with one of these therapeutic agents, or that capecitabine 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.

On November 19, 2014, the FDA approved Genentech, Inc.'s supplemental Biologics License Application for Avastin plus chemotherapy for the treatment of women with recurrent platinum-resistant ovarian cancer. This approval may alter the regulatory and commercial landscape of ovarian cancer drug development. We are commencing start-up activities for a Company-sponsored Phase 1b trial with the GOG Foundation, Inc. in which we will evaluate the combination of CRLX101 with weekly paclitaxel in patients with relapsed ovarian cancer. Based on the data generated by that trial, we will further evaluate the regulatory requirements and the commercial opportunity for CRLX101 in relapsed ovarian cancer. It is possible that we will determine that the threshold for regulatory approval is too high or that the commercial opportunity is too narrow and, for either reason, we might abandon our efforts to develop CRLX101 in relapsed ovarian cancer.

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-1 a 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.

Two of our product candidates are in clinical development, all of our other potential product candidates are in preclinical development, and the risk of failure of all of our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to 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 Phase 2 clinical trials for patients with advanced NSCLC who had progressed through one or two prior regimens of chemotherapy, CRLX101 failed to meet its primary endpoint of improvement in overall survival of patients in this indication. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face additional setbacks. 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 RCC; a two-part Phase 2 open-label IST in patients with relapsed ovarian cancer, consisting of a single-arm trial of CRLX101 as monotherapy and a single-arm combination trial of CRLX101 and Avastin; and a Phase 1b/2 open-label IST of CRLX101 in combination with chemoradiotherapy in patients with neoadjuvant rectal cancer. Interim investigator-reported data from subsets of the total patient populations in certain of these ISTs have been reported. These ISTs are still in progress and final results are not yet available. The preliminary results reported from the ISTs have in some cases been observed in only a small number of patients and may not be achieved by other patients on these or other clinical trials. There can be no assurance that company-sponsored trials will confirm the data seen in the ISTs.

The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed. 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, variability in the quality of clinical supply batches and the rate of dropout among clinical trial participants. Any Phase 2, Phase 3 or other clinical trials that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates.

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

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

- clinical trials of our product candidates may produce unfavorable 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;
- investigators may deviate from the trial protocol, fail to conduct the trial in accordance with regulatory requirements or misreport study data;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- prospective clinical trial sites may be unwilling to participate in one or more of our combination clinical trials due to a perceived difficulty in obtaining reimbursement from managed care plans, government, or other third party payors;
- patients who enroll in a clinical trial, or the investigators enrolling such patients, may misrepresent the patients' eligibility to participate in the trial or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- for any given trial we may find it necessary to open more clinical trial sites than originally planned;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, unexpected or serious adverse events or other unexpected characteristics of a product candidate;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their respective standards of conduct, a finding that the participants are being exposed to unacceptable health risks, unexpected or serious adverse events or other unexpected characteristics of the product candidate or other therapeutic agents used in our clinical trials or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;
- the FDA or comparable non-U.S. regulatory authorities may disagree with our clinical trial design or our interpretation of data from preclinical studies and clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- the FDA or comparable non-U.S. regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we enter into agreements for clinical and commercial supplies;

- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable non-U.S. regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

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

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

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

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 good clinical practice, including review and approval by an independent ethics committee and informed consent from subjects. 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 which we intend to seek approval in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. 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 Phase 1/2a clinical trial of CRLX301 in Australia, for example, or any other trial that we conduct outside the United States, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay or permanently halt our development of CRLX101, CRLX301 or any future product candidates.

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

- foreign regulatory requirements that could burden or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations;
- manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; 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, or (4) there are unacceptable safety concerns associated with our product candidates, we, in addition to incurring additional costs, may:

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

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

We may to seek fast track designation for some of our product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

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

We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

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

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

A ten month standard NDA review clock will begin at the conclusion of the 60 calendar day filing review period that starts on the date of FDA receipt of the original submission. This results in a total of twelve months until the FDA is to take regulatory action. We may be eligible for Priority Review designation for our NDA submission if the FDA determines that our product candidate treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The six month Priority Review clock will begin at the conclusion of the 60 calendar day filing review period that starts on the date of FDA receipt of the original submission. Therefore, if granted Priority Review, the FDA has a total of eight months to take action on an application rather than the total of twelve months for a standard review from their receipt of the original submission. 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 product candidates, 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 also does not guarantee approval within the eight-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 registration pathways. If unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals.

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

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

A failure to obtain Accelerated Approval or any other form of expedited development, review or approval for our product candidates would result in a longer time period to 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 of CRLX101 or any of our product candidates may be identified during clinical development. Further, other unexpected properties of our product candidates may be identified during manufacture or development. Such adverse events or unexpected properties could delay or prevent the continued development and/or marketing approval of any such product candidate.

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

Both camptothecin, the anti-cancer payload of CRLX101, and docetaxel, the anti-cancer payload of CRLX301, have been associated with toxicities. These toxicities led to discontinuation of the clinical development in the case of camptothecin and have led to dose adjustments, treatment discontinuation and extensive supportive care in the case of docetaxel. While we believe that our Dynamic Tumor Targeting Platform has the potential to improve the unfavorable adverse event profiles of both camptothecin and docetaxel, if this hypothesis is wrong and we experience unexpected or more severe toxicities in our ongoing clinical trials or in clinical trials we conduct in the future, whether due to the inclusion of camptothecin or docetaxel or another therapeutic as the anti-cancer payload in our NDCs or otherwise, we may not receive approval to market, or achieve commercial success with respect to, any of our product candidates, which could prevent us from ever generating revenues or achieving profitability. In addition, our Dynamic Tumor Targeting Platform may have other limitations with respect to targeting tumors and limiting exposure of normal tissue to our NDCs' anti-cancer payload. For example, liver tissue has pore sizes that are generally larger than other normal tissue, and therefore, our NDCs and their anti-cancer payloads may preferentially concentrate in the liver.

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

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

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

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 may not become profitable. The degree of market acceptance of CRLX101 or any of our other product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- our ability to offer the product for sale at competitive prices;
- our ability to establish and maintain pricing sufficient to realize a meaningful return on our investment;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- the strength of sales, marketing and distribution support;
- the availability of alternative treatments already approved or approval of other new products for the same indications;
- changes in the standard of care for the targeted indications for the product;
- the timing of market introduction of our approved products as well as competitive products and other therapies;
- availability and amount of reimbursement from government payors, managed care plans and other third party payors;
- the strength and efficacy of our marketing and distribution efforts;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

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

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

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

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we may be required to recall the drug or change the way the drug is administered;

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

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

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

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

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

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

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

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

Several companies are marketing and developing oncology products. Companies with marketed nanoparticle oncology products include Celgene Corporation (Abraxane indicated for breast cancer, NSCLC and pancreatic cancer), Janssen (Doxil® for ovarian cancer and, in combination with botezomib, for multiple myeloma) and Spectrum Pharmaceuticals (Marqibo ® (vincristine sulfate liposome injection) indicated for relapsed Philadelphia chromosome-negative acute lymphoblastic leukemia). Companies with nanoparticle oncology product candidates in clinical development include BIND Therapeutics, Inc. (BIND 014 for NSCLC and metastatic castration-resistant prostate cancer), Nippon Kayku Seizo Co., Ltd. (NK105 in breast 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 product candidates before we are able to obtain approval for our product candidates, which could result in our competitors establishing a strong market position before we are able to enter the market. The competition for CRLX101 in our targeted indications includes the following:

Renal Cell Carcinoma. In advanced RCC, several drugs in development have the potential to obtain FDA marketing approval and change the standard of care. If this occurs, currently available treatments could be replaced or altered and our commercial opportunity could be reduced. For example, Exelixis, Inc. is developing cabozantinib in advanced RCC and the data from its ongoing phase 3 trial are anticipated in 2015. Acceleron Pharma Inc. is developing dalantercept in combination with axitinib, and TRACON Pharmaceuticals, Inc. is developing TRC105, also in combination with axitinib.

In addition to these tyrosine kinase inhibitor and tyrosine kinase inhibitor combination programs in advanced RCC, immune checkpoint inhibitors, including nivolumab and pembrolizumab, are also being developed in RCC. Although these product candidates are being tested for earlier lines of therapy, they also have the potential to change the standard of care in advanced RCC, which, among other things, could result in existing first line therapies being prescribed instead for later lines of therapy. If this occurs, it would potentially reduce the commercial opportunity for CRLX101 in relapsed RCC.

Relapsed Ovarian Cancer. In relapsed ovarian cancer, the recent FDA approvals of Avastin with chemotherapy and Lynparza® in BRCA mutated patients has changed the standard of care, which could reduce the commercial opportunity for CRLX101.

Neoadjuvant Rectal Cancer. In neoadjuvant rectal cancer, Isofol Medical AB is developing a molecule that is currently labeled [6R] 5,10-methylenetetrahydrofolate; Karyopharm Therapeutics Inc. is developing Selinexor in combination with chemoradiotherapy; Merck KGaA is developing tecemotide with chemoradiotherapy; Genentech, Inc. is testing Avastin in combination with capecitabine; and Kadmon Corporation, LLC is developing KD018 in combination with capecitabine and radiation. If any of these product candidates receives marketing approval, our commercial opportunity in neoadjuvant rectal cancer could be reduced.

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

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

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

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

There is significant uncertainty related to third party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some non-U.S. markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy 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 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 $7.5 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 patient enrollment in, or the timing and reporting of the data from, ISTs, nor do we own the data from the ISTs. Moreover, if we are unable to confirm or replicate the results from the ISTs or if negative results are obtained in the ISTs, we would likely be further delayed or prevented from advancing further clinical development of our drug candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our drug candidates, or if the data proves to be 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 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, also referred to as 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 required several months to 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 or result in our inability to generate sufficient supplies to meet commercial demands. 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 or should be unable to secure additional manufacturing capacity in the event of higher than anticipated product demand, we may incur additional cost or delay in identifying or qualifying replacements. In addition, while we believe that our existing supplier of drug substance or an alternative supplier would be capable of continuing to produce drug substance in commercial quantities, we will need to identify a third-party manufacturer capable of providing commercial quantities of drug product. If we are unable to arrange for such a third-party manufacturing source, or fail to do so on commercially reasonable terms, we may not be able to successfully produce and market CRLX101 or any other product candidate or may be delayed in doing so.

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

- reliance on the third party for regulatory compliance and quality assurance;
- the ability of manufacturers to consistently produce intermediates, drug substance or drug product that meet required quality specifications;
- the possible breach of the manufacturing agreement by the third party;

- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

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

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

In addition, we 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. 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 USPTO, recently developed new regulations and procedures to govern administration of the Leahy-Smith Act. However, many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or licensed patent applications and the enforcement or defense of our owned or licensed issued patents, all of which could have a material adverse effect on our business and financial condition.

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

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

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

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

Competitors may infringe our owned or licensed patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file or participate in infringement claims, which can be expensive and time consuming. Any claims we or our licensors assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensor is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or licensed patents at risk of being invalidated or interpreted narrowly.

CRLX101 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 NDCs, such as CRLX301. In addition, we hold an exclusive license from the Massachusetts Institute of Technology, or MIT, for polymeric NDC-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. On March 3, 2015, Calando's bankruptcy trustee submitted an application with the bankruptcy court seeking authority to retain a broker to sell Calando's rights in certain assets including its rights in the license agreements with Cerulean. We have reserved our rights with respect to any such sale.

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 agreements are terminated, our former licensors and/or assignors may be able to prevent us from utilizing the technology covered by the licensed or assigned patents and patent applications. For example, under our agreements with Calando, which relate to CRLX101 and our 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 multiple intellectual property agreements that impose, and we may enter into additional intellectual property agreements that may impose, various diligence, milestone payment, royalty and other obligations on us. Under our existing intellectual property agreements, we are obligated to pay royalties on the net sales of product candidates or related technologies to the extent they are covered by the agreement. We also have diligence and development obligations under those agreements. If we fail to comply with our obligations under current or future intellectual property agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product that is covered by the agreement or face other penalties under the agreement. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

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

Some of the intellectual property rights we have licensed may have been generated through the use of United States government funding and may therefore be subject to certain federal regulations. For example, some of the intellectual property rights licensed to us under the MIT agreement, and which are relevant to our PNP-based NDCs, 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 NDCs such as CRLX301 may have been generated using United States government funds. As a result, the United States government may have certain rights to intellectual property embodied in 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. For example, if the regulatory landscape in the United States, Europe or Asia shifts unexpectedly, it may adversely affect the feasibility of study arms, standards of care or statistical assumptions currently reflected in our clinical development plans for CRLX101, potentially delaying the development of CRLX101 in a particular indication and increasing the time required to obtain marketing approval for CRLX101.

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 governing the labeling, packaging, storage and promotion of the product and record keeping and submission of safety and other post-market information.

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

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive 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 regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market our products for unapproved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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

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

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

Our relationships with 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;
- 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

We are operating under a transitional management team following the resignation of our former president and chief executive officer.

Dr. Oliver Fetzer, our former president, chief executive officer and director, resigned from his positions effective October 29, 2014. We anticipate that we will continue to experience a transitional period until our new chief executive officer is hired and then fully integrated into his or her new roles.

In connection with Dr. Fetzer's resignation, Paul A. Friedman, M.D., a member of our board of directors, was appointed Executive Chairman of our board and Christopher D.T. Guiffre was appointed as our Chief Operating Officer. Mr. Guiffre is serving as the Company's principal executive officer.

We cannot predict how long it will take to find a new chief executive officer and it is possible that we will operate with a transitional leadership team for an extended period. If we are not able to appoint a new president and chief executive officer in a timely manner, or if either Dr. Friedman or Mr. Guiffre ceases to fulfill his respective new role during the transitional period, our business, financial condition, and results of operations could be materially and adversely affected. Moreover, we cannot provide any assurance that this transitional period will not result in a disruption that adversely impacts our business and employee morale.

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 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 finance 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, including finance personnel, may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific 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.

Our existing lease will expire in February 2016. If we elect not to exercise our extension right under this lease and are unable to lease suitable space, our need to relocate our facilities could delay our research and development efforts, adversely affect our business and damage employee morale.

We lease laboratory and office space in Cambridge, Massachusetts under a lease expiring on February 29, 2016. We have the right to extend the lease for an additional three year term, subject to reaching agreement with the landlord on market rent for the term of the extension. Our landlord is attempting to sell the building in which we are located, and the efforts to sell the building may make it more difficult for us to reach an agreement on the market rent for the term of the extension. If we elect not to exercise our extension right, or are not able to reach agreement on market rent for the term of the extension, we will need to relocate our laboratory and office space. In these circumstances, we may be unable to obtain alternative facilities due to our financial condition or for other reasons, and we may be unable to fully relocate our existing operations before termination of our existing lease, thereby disrupting our business and research and development activities. In the event that we relocate to a new location, the new location we choose may adversely affect employee retention or recruitment, and the process of moving our offices to a new location may disrupt our operations.

Risks Related to our Common Stock

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

Our stock price has been and may in the future be volatile. From April 10, 2014 to February 28, 2015, the sale price of our common stock as reported on the NASDAQ Global Market ranged from a high of $8.44 per share to a low of $3.35 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- actual or anticipated results from, and any delays in, our clinical trials, including the ongoing and any new ISTs of CRLX101, our ongoing and planned Phase 2 and Phase 3 clinical trials of CRLX101 or our 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 executive officers and directors and their affiliates own a significant percentage of our stock and will be able to exercise significant influence over matters submitted to stockholders for approval.

We believe that as of February 28, 2015, our executive officers and directors and their affiliates will own 37.2% of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to exert a significant degree of influence over matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would substantially influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership could:

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

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

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

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

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

As of December 31, 2014, there were 2,126,186 shares subject to outstanding options. In August 2014, we registered all of these shares under the Securities Act of 1933, as amended, on a registration statement on Form S-8. These shares can be freely sold in the public market upon exercise, as permitted by any applicable vesting requirements, except to the extent they are held by our affiliates, in which case such shares will become eligible for sale in the public market as permitted by Rule 144 under the Securities Act. Furthermore, as of December 31, 2014, there were 128,663 shares subject to outstanding warrants to purchase common stock. These shares will become eligible for sale in the public market, to the extent such warrants are exercised, as permitted by Rule 144 under the Securities Act. Moreover, holders of approximately 6.9 million shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

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

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

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

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

- 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 cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

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

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

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

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

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

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

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

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

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

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

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

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

Our principal facilities consist of approximately 23,000 square feet of office and laboratory space located at 840 Memorial Drive, Cambridge, Massachusetts. The lease expires in February 2016, subject to our option to extend the lease for an additional three years.

Item 3. ***Legal Proceedings***

In March 2014, Calando Pharmaceuticals, Inc., or Calando, entered Chapter 7 bankruptcy in the District of Delaware 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. On March 3, 2015 Calando's bankruptcy trustee submitted an application with the bankruptcy court seeking authority to retain a broker to sell Calando's rights in certain assets including its rights in the license agreements with Cerulean. We have reserved our rights with respect to any such sale.

Item 4. ***Mine Safety Disclosures***

None.

PART II

Item 5. ***Market for Registrant's Common Shares, Related Stockholder Matters and Issuer Purchases of Equity Securities***

Market Information

Our commons stock has been listed on the NASDAQ Global Market under the symbol "CERU" since April 2014. The following table sets forth on a per share basis, for the periods indicated, the low and high sale prices of our common stock as report by the NASDAQ Global Market.

	Year Ended December 31, 2014	
	High	Low
Second Quarter (from April 10, 2014)	$ 8.06	$ 5.05
Third Quarter	$ 7.30	$ 3.35
Fourth Quarter	$ 6.45	$ 3.95

Holders

As of the close of business on March 16, 2015, there were approximately 54 holders of record of our common stock.

Dividend Policy

We have never declared or paid cash dividends on our common stock. We currently intend to retain any current and future earnings to finance the growth and development of our business and, therefore, do not anticipate paying any cash dividends in the foreseeable future. Our amended and restated credit facility contains restrictions on our ability to pay dividends.

Purchases of Equity Securities by the Issuer and Affiliated Purchaser

None.

Use of Proceeds

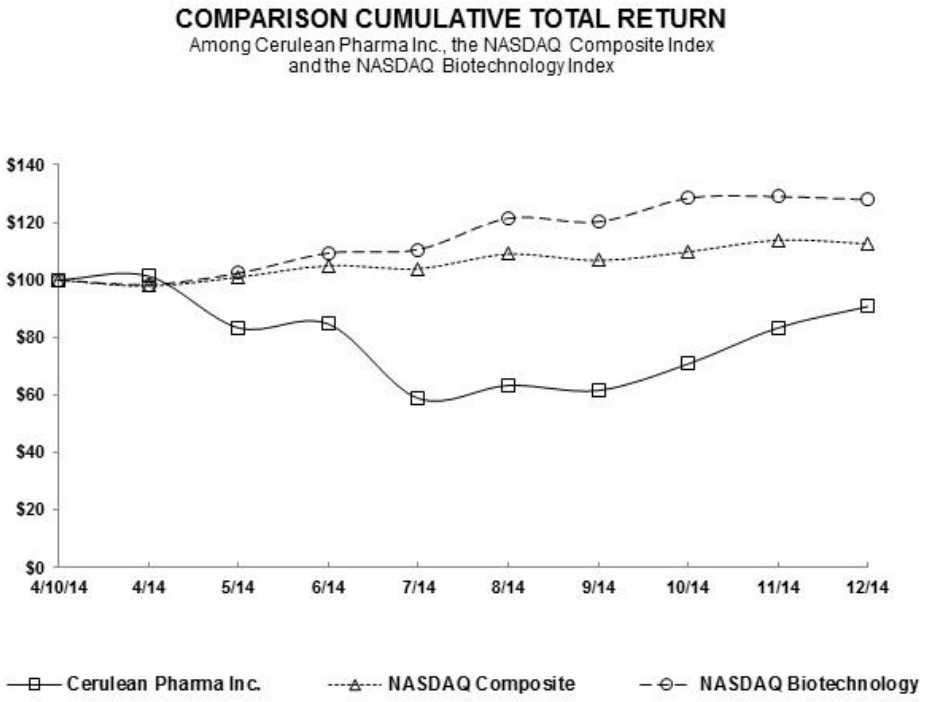
On April 15, 2014, we completed the sale of 8,500,000 shares of our common stock in our IPO at a public offering price of $7.00 per share. On May 7, 2014, we completed the sale of an additional 1,069,715 shares of common stock at a public offering price of $7.00 per share, pursuant to a partial exercise by the underwriters of their option to purchase additional shares of common stock. All of the shares issued and sold in our IPO were registered under the Securities Act of 1933, as amended, pursuant to a Registration Statement on Form S-1 (File No. 333-194442), which was declared effective by the Securities and Exchange Commission on April 10, 2014.

The net offering proceeds to us, after deducting underwriting discounts and offering expenses payable by us were approximately $59.9 million. As of December 31, 2014, we have used approximately $8.7 million of the net proceeds from our IPO for research and development of our programs, working capital and other general corporate purposes. None of the net proceeds were paid directly or indirectly to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any affiliates of ours, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for board or board committee service. We have invested the net proceeds from the offering in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities. There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on April 14, 2014.

Performance Graph

This performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended ("Exchange Act"), or otherwise subject to the liabilities under that section, and shall not be deemed to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act.

The following graph compares the cumulative total return to stockholders for the our common shares for the period from April 10, 2014 through December 31, 2014 with The NASDAQ Composite Index and the NASDAQ Biotechnology index (NBI). The comparison assumes an investment of $100 is made on April 10, 2014 in the Company's common shares and in each of the indices and in the case of the indices it also assumes reinvestment of all dividends. The performance shown is not necessarily indicative of future performance.



Item 6. ***Selected 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 Annual Report on Form 10-K. We have derived the consolidated statements of operations data for the years ended December 31, 2014, 2013 and 2012, and the consolidated balance sheet data at December 31, 2014 and 2013 from our audited consolidated financial statements included in this report on Form 10-K. The consolidated balance sheet data as of December 31, 2012 are from our audited consolidated financial statements that are not in this Form 10-K. Our historical results for any prior period are not necessarily indicative of the results to be expected in any future period.

	Years Ended December 31,		
(in thousands, except share data and per share data)	2014	2013	2012
Consolidated Statement of Operations Data:			
Revenue	$ 80	$ 6	$ 625
Operating expenses:			
Research and development	11,772	9,700	15,807
General and administrative	8,587	6,166	6,393
Total operating expenses	20,359	15,866	22,200
Other income (expense):			
Interest income	9	2	2
Interest expense	(1,083)	(1,487)	(567)
Loss on extinguishment of debt	(2,493)	-	-
Decrease in value of preferred stock warrant liability	504	202	39
Total other (expense)—net	(3,063)	(1,283)	(526)
Net loss	(23,342)	(17,143)	(22,101)
Accretion of redeemable convertible preferred stock	—	—	(73)
Net loss attributable to common stockholders	$ (23,342)	$ (17,143)	$ (22,174)
Net loss per share attributable to common stockholders:			
Basic and diluted	$ (1.60)	$ (25.05)	$ (36.39)
Weighted-average common shares outstanding:			
Basic and diluted	14,548,516	684,330	609,344

	As of December 31,		
(in thousands)	2014	2013	2012
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 51,174	$ 5,488	$ 16,707
Working capital (deficit)	$ 44,775	$ (8,699)	$ 10,540
Total assets	$ 53,393	$ 6,827	$ 17,661
Long-term debt (including current portion)	$ 3,124	$ 6,258	$ 9,127
Redeemable convertible preferred stock	$ -	$ 81,525	$ 83,751
Common stock	$ 2	$ -	$ -
Additional paid in capital	$ 167,104	$ 4,140	$ 1,257
Accumulated deficit	$ (121,781)	$ (98,439)	$ (81,296)
Total stockholders' equity (deficit)	$ 45,325	$ (94,299)	$ (80,039)

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our condensed consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, 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 Annual Report on Form 10-K 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. This platform utilizes nanoparticle-drug conjugates, or NDCs, which consist of proprietary polymers that are covalently linked to anti-cancer therapeutics, or payloads. We believe these NDCs 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. We believe that our NDCs are differentiated from other nanoparticle technologies by our linker technology, which allows for preferential delivery of our anti-cancer payloads.

Our lead product candidate, CRLX101, is a dynamically tumor targeted NDC in Phase 2 clinical development and has the potential to improve outcomes for patients in combination with other cancer treatments. 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. Two products that have been marketed by other companies, irinotecan and topotecan, inhibit topo 1, but their utility is limited by toxicities. Recent research suggests that HIF, and in particular the HIF subunit HIF-lα, is a master regulator of multiple cancer cell survival pathways. Over 250 patients have been administered CRLX101 in multiple indications at several clinical trial sites. In clinical trials evaluating CRLX101 as a single agent, CRLX101 was generally well tolerated with a toxicity profile generally characterized by low-grade (Common Terminology Criteria for Adverse Events grade 1-2) adverse events. No treatment-related trial deaths have been observed to date. In ongoing clinical trials, CRLX101 also appears active and combinable with Avastin (bevacizumab) and chemoradiotherapy, or CRT, which is a combination of capecitabine and radiation. In addition, preclinical data indicate that CRLX101 may be combinable with other anti-cancer therapies. We are pursuing development of CRLX101 in combination with anti-cancer therapies in multiple ongoing clinical development programs that include a company-sponsored trial and investigator-sponsored trials, or ISTs. These trials consist of:

- *Relapsed renal cell carcinoma:*

    - A Phase 2 randomized, controlled, company-sponsored trial is being conducted comparing CRLX101 administered in combination with Avastin to investigator's choice of standard of care in patients with renal cell carcinoma, or RCC, who have received two or three prior lines of therapy. We refer to this study as the RCC Trial. The RCC Trial is currently being conducted at approximately 30 sites in the United States, with eight additional sites planned in the United States and five additional sites planned in South Korea. Based on results from the Phase 1b/2 IST in relapsed RCC, discussed below, we believe that the combination of CRLX101 and Avastin may provide therapeutic benefits to patients with RCC who have received two or three prior lines of therapy including a tyrosine kinase inhibitor, or TKI, and/or an inhibitor of a mammalian target of rapamycin, or an mTORI.

    - A Phase 1b/2 single-arm IST of CRLX101 in combination with Avastin in patients with relapsed RCC is being conducted at the University of Pennsylvania and Thomas Jefferson University Hospital. A total of 22 patients were enrolled in this trial. The last patient was enrolled in December of 2014, and the trial has met its primary endpoint of at least 50% of patients achieving four months progression free survival, or PFS. Preliminary data from this clinical trial has been submitted for presentation at the 2015 annual meeting of the American Society of Clinical Oncology, or ASCO. As of February 3, 2015, the date of the abstract submission to ASCO, the median PFS, or mPFS, of patients on the trial was 9.9 months, with seven of the 22 patients still receiving treatment. Based on third-party published data, the mPFS of the standard of care in this setting is approximately 3.5 months. In addition, the Response Evaluation Criteria in Solid Tumor, or RECIST, partial response rate of patients on the trial as of February 3, 2015 was 23%. Several recent studies in advanced RCC suggest that after treatment with a TKI, subsequent therapies, including Avastin alone, achieve RECIST partial response rates of only between 2% and 4%.

- *Relapsed ovarian cancer:*

    - A Phase 2 single-arm IST of CRLX101 as monotherapy and in combination with Avastin in patients with relapsed ovarian cancer is being conducted at Massachusetts General Hospital and affiliated Harvard University teaching hospitals. As previously reported, the first stage of the trial, administering CRLX101 as monotherapy, met its primary endpoint of PFS at six months for at least four patients. RECIST responses, as well as encouraging PFS, were observed for several patients. Platinum-resistant ovarian cancer patients are being enrolled in the second stage of this trial, administering CRLX101 in combination with Avastin.

    - We have commenced start-up activities for a Phase 1b single-arm company-sponsored trial of CRLX101 in combination with weekly paclitaxel in patients with relapsed ovarian cancer conducted in collaboration with the GOG Foundation, Inc. (formerly known as the Gynecologic Oncology Group), or GOG.

- *Neoadjuvant rectal cancer:*

    - A Phase 1b/2 single-arm IST of CRLX101 in combination with CRT in patients with non-metastatic rectal cancer is being conducted at the University of North Carolina at Chapel Hill and several other sites, including the University of Indiana, Wake Forest University, Rex Hospital Inc. and Southeastern Medical Oncology Center. No dose limiting toxicities, or DLTs, have been reported in the Phase 1b stage of the trial, in which a maximum tolerated dose, or MTD, and recommended Phase 2 dose, or RP2D, of 15 mg/m2 of CRLX101 was established when administered in combination with capecitabine and radiotherapy. Patients are currently being enrolled in the RP2D expansion Phase 2 stage of the trial.

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 ability of NDCs to target the "leaky" vasculature that is present in all solid tumors 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 other cancer therapies. Our development focus is on tumor types where HIF is up-regulated, topo 1 inhibition is desirable, and drug combinations with CRLX101 can be pursued.

CRLX301, our second platform-generated clinical candidate, is a dynamically tumor-targeted NDC in Phase 1 clinical development. CRLX301 is designed to concentrate in tumors and slowly release its anti-cancer payload, docetaxel, inside tumor cells. Docetaxel is a microtubule stabilizer that is extensively used in clinical practice and is approved by the FDA for the treatment of locally advanced or metastatic non-small cell lung cancer, locally advanced squamous cell carcinoma of the head and neck, androgen-independent prostate cancer, locally advanced or metastatic breast cancer and advanced gastric cancer. In preclinical studies, CRLX301 delivered up to ten times more docetaxel into tumors, compared to an equivalent milligram dose of commercially available docetaxel and was superior to docetaxel in seven of seven animal models, with a statistically significant survival benefit seen in five of the seven models. In addition, preclinical data show that CRLX301 had lower toxicity than has been reported with docetaxel in similar preclinical studies. 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.

Our proprietary Dynamic Tumor Targeting Platform utilizes cyclodextrin polymer, or CDP, technology, which is primarily used for creating NDCs that contain small molecules such as camptothecin in the case of CRLX101 and docetaxel in the case of CRLX301. In addition to CRLX101 and CRLX301, we have generated additional NDCs 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.

We have devoted substantially all of our resources to our drug discovery and development efforts, including conducting clinical trials of our product candidates, protecting our intellectual property and the general and administrative support of 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, 2014, we have funded our operations primarily through $84.2 million in proceeds from the sale of shares of our convertible preferred stock in private placements, net proceeds of $59.9 million from sales of shares of our common stock to the public, $17.3 million in proceeds from our sale of convertible promissory notes, and $10.0 million in proceeds from borrowings under our loan and security agreement with Lighthouse Capital Partners VI, L.P., or Lighthouse Capital. We refer to our loan and security agreement with Lighthouse Capital as the Lighthouse Loan Agreement.

On January 8, 2015, we entered into a loan and security agreement with Hercules Technology Growth Capital, Inc., or Hercules. We refer to this loan and security agreement as the Hercules Loan Agreement. Pursuant to the Hercules Loan Agreement, we are eligible to borrow up to an aggregate principal amount of $26.0 million, subject to certain conditions. On January 8, 2015, we

borrowed $15.0 million under the Hercules Loan Agreement, and we used a portion of those proceeds to repay our outstanding indebtedness under the Lighthouse Loan Agreement. In connection with entering into the Hercules Loan Agreement, we sold 135,501 shares of our common stock to Hercules in a private placement and received $1.0 million in proceeds.

We have never been profitable and have incurred significant operating losses since our incorporation. As of December 31, 2014, we had an accumulated deficit of $121.8 million. We incurred net losses of approximately $23.3 million, $17.1 million and $22.2 million for the years ended December 31, 2014, 2013, and 2012, respectively.

We expect to continue to incur significant and increasing expenses and operating losses for the foreseeable future, as we 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.

Initial Public Offering

On April 15, 2014, we completed the sale of 8,500,000 shares of common stock in our initial public offering, or IPO, at a price to the public of $7.00 per share. On May 7, 2014, we completed the sale of an additional 1,069,715 shares of common stock at a price to the public of $7.00 per share, pursuant to a partial exercise by the underwriters of their option to purchase additional shares of common stock. The sale of the shares to the public resulted in aggregate net proceeds to us of $59.9 million after deducting underwriting discounts and commissions and offering expenses payable by us.

In addition, each of the following occurred in the second quarter of 2014 in connection with the completion of our IPO on April 15, 2014:

- the conversion of all outstanding shares of convertible preferred stock into 6,826,004 shares of our common stock;
- the conversion of $17.8 million of outstanding principal and accrued interest on convertible notes into 2,902,233 shares of our common stock; and
- the conversion of warrants to purchase 1,857,226 shares of convertible preferred stock into warrants to purchase 128,663 shares of our common stock and the reclassification of the $0.4 million warrant liability to additional paid-in capital.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the next several years, if ever. In the future, we may generate revenue from a combination of product sales, license fees, milestone and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of any such payments. Our ability to generate product revenues will depend on the successful development and eventual commercialization of our product candidates and our dynamic tumor targeting technology. If we fail to complete the development of our product candidates in a timely manner, to fully realize the value and potential of our technology platform, 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 we received in 2011, 2012, 2013, and 2014 from four material transfer agreements and a research agreement. Pursuant to each of the agreements, we received payments in exchange for a pharmaceutical company’s use of our proprietary technology for research purposes.

Research and Development Expenses

Research and development expense consists of costs incurred in connection with the discovery and development of our Dynamic Tumor Targeting Platform and our 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, or CROs, investigative sites that conduct our clinical trials and consultants that conduct a portion of our preclinical studies;

- expenses relating to scientific and medical consultants and advisors;
- the cost of acquiring and manufacturing clinical trial materials;
- facilities, depreciation of fixed assets and other allocated expenses, including direct and allocated expenses for rent and maintenance of facilities and equipment;
- lab supplies, reagents, active pharmaceutical ingredients and other direct and indirect costs in support of our preclinical activities;
- license fees related to in-licensed products and technology; and
- costs associated with non-clinical activities and regulatory approvals.

We expense research and development costs as incurred.

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

We use our employee and infrastructure resources across multiple research and development programs. We track external research and development expenses and personnel expense on a program-by-program basis and have allocated expenses such as stock-based compensation and indirect laboratory supplies and services to each program based on the personnel resources allocated to each program. Facilities, depreciation and scientific advisory board fees and expenses are not allocated to a program and are considered overhead. Below is a summary of our research and development expenses for the years ended December 31, 2014, 2013 and 2012 (in thousands):

	Years Ended December 31,		
	2014	2013	2012
CRLX101	$ 7,235	$ 4,655	$ 8,379
CRLX301	2,446	2,299	3,792
NDC platform	1,212	2,007	2,618
Overhead	879	739	1,018
Total research and development expense	$ 11,772	$ 9,700	$ 15,807

The following summarizes our research and development programs.

CRLX101

CRLX101 is currently being studied in multiple clinical trials, including the RCC Trial and the three ISTs described above. We expect to conduct additional trials of CRLX101, including a Phase 1b trial of CRLX101 in combination with weekly paclitaxel in patients with relapsed ovarian cancer, which we will conduct in collaboration with GOG.

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

CRLX301

CRLX301 is currently in early stage clinical development, with a Phase 1 trial ongoing. Assuming we are successful in establishing a safe maximum tolerated dose, or MTD, and/or a recommended Phase 2 dose in the Phase 1 trial, we plan to rapidly advance CRLX301 into Phase 2 development.

Under our license agreement with Calando pursuant to which we obtained rights to Calando's cyclodextrin system for purposes of conjugating or complexing certain other therapeutic agents to the system, or the Platform Agreement, we paid a $250,000 clinical development milestone to Calando in January 2015 in connection with the initiation of our Phase 1 clinical trial of CRLX301 in December 2014. We may also be required to make milestone payments in an aggregate amount of up to $18.0 million to Calando if we achieve certain development and sales events with respect to any CDP-based product. Further, under the Platform Agreement, if we, or one of our affiliates, sell CRLX301, or any CDP-based product, we are required to pay tiered royalty payments ranging from low- to mid-single digits, as a percentage of worldwide net sales, depending on whether there is patent protection at the time of the sale. In the event we license or sublicense the intellectual property that we purchased or licensed from Calando, we are required to pay Calando a percentage of the income we receive from the licensee or sublicensee to the extent attributable to such license or sublicense, subject to certain exceptions. The percentage of such license income that we are obligated to pay Calando is in the low-double digits.

Nanoparticle-Drug Conjugates

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

The successful development of any of our 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 development of our product candidates will depend on a variety of factors, including:

- the scope and rate of progress of our ongoing clinical trials;
- a continued acceptable safety profile of any product candidate once approved;
- the scope, progress, timing, results and costs of researching and developing our product candidates, and conducting preclinical and clinical trials;
- results from ongoing as well as any future clinical trials;
- significant and changing government regulation in the United States and abroad;
- the costs, timing and outcome of regulatory review or approval of our product candidates in the United States and abroad;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- establishment of arrangements with third party suppliers or raw materials and third party manufacturers of finished drug product;
- 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 data with respect to 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, if any.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and related costs for personnel in our executive, finance, business development, marketing, legal 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 will continue to increase as a result of increased payroll, expanded infrastructure, higher consulting, legal, accounting and investor relations costs, director compensation and director and officer insurance premiums associated with being a public company; and

- we may begin to incur expenses related to sales and marketing of our 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 interest expense on our convertible notes and our debt facility with Lighthouse Capital.

Loss on Extinguishment of Debt

Loss on extinguishment of debt is associated with the loss recorded on the conversion of the convertible notes we issued in 2014, or the 2014 Convertible Notes. The loss is an amount equal to the difference between the fair value of shares of our common stock into which the 2014 Convertible Notes converted and the carrying amount of the 2014 Convertible Notes at the closing of the IPO on April 15, 2014.

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. The preferred stock warrants were automatically adjusted on the date of the closing of the IPO, April 15, 2014, to provide for the issuance of shares of common stock upon their exercise. The preferred stock warrant liability has been reclassified to additional paid-in capital as of April 15, 2014.

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 Annual Report on Form 10-K. 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 CROs 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 trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials 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. We have not experienced any significant adjustments to our estimates to date.

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 performance-based grants where the vesting of the grant is tied to certain milestone performance and, in these cases, the compensation is recognized as expense when the probability of the milestone is met. 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 for recording stock-based compensation expense using the Black-Scholes option pricing model. Determining the appropriate fair value model and calculating the fair value of stock-based awards requires significant judgment and the use of assumptions.

Prior to our IPO, we were a private company with no active public market for our common stock. Therefore, we 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 did not always coincide 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 90 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.

There were significant judgments and estimates inherent in the determination of fair value of our common stock, including the contemporaneous valuations. These judgments and estimates included assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event and the determinations of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per common share could have been significantly different.

Since our IPO, we have determined the fair value of our common stock based on the closing price of our common stock on The NASDAQ Global Market on the applicable date of such grant.

Determination of Fair Market Value of Common Stock Prior to IPO

Common Stock Valuation Methodologies

Prior to our IPO, our 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.

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2013

The following table summarizes our consolidated results of operations for the years ended December 31, 2014 and 2013, together with the changes in those items in dollars and as a percentage (in thousands, except percentages):

	Years Ended December 31,		Change	
	2014	2013	Dollar	%
Revenue	$ 80	$ 6	$ 74	*
Operating expenses:				
Research and development	11,772	9,700	2,072	21%
General and administrative	8,587	6,166	2,421	39%
Loss from operations	(20,279)	(15,860)	(4,419)	28%
Other income/(expense), net	(3,063)	(1,283)	(1,780)	*
Net loss	$ (23,342)	$ (17,143)	$ (6,199)	36%

* Not meaningful

Revenue. For the year ended December 31, 2014 revenue was $80,000 compared to $6,000 for the year ended December 31, 2013. For both periods, revenue is from two material transfer agreements and reflects timing of activity and payments received under the agreements.

Research and development. The following table summarizes our research and development expense by program for the years ended December 31, 2014 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	
	2014	2013	Dollar	%
CRLX101	$ 7,235	$ 4,655	$ 2,580	55%
CRLX301	2,446	2,299	147	6%
Dynamic Tumor Targeting platform	1,212	2,007	(795)	(40)%
Overhead	879	739	140	19%
Total research and development expense	$ 11,772	$ 9,700	$ 2,072	21%

Research and development expense for the year ended December 31, 2014 was $11.8 million compared to $9.7 million for the year ended December 31, 2013, an increase of $2.1 million, or 21%. The increase was primarily attributable to an increase in costs associated with the CRLX101 program and partially offset by lower costs associated with our Dynamic Tumor Targeting Platform new discovery research.

For the year ended December 31, 2014, costs associated with the CRLX101 program increased $2.6 million, or 55%, to $7.2 million from $4.6 million for the year ended December 31, 2013. The increase was primarily due to ongoing costs associated with the RCC Trial. CRLX101 clinical trial expenses increased by $2.0 million in 2014 compared to the prior year as a result of increased costs for our CRO and laboratories, as well as clinical site initiation costs and patient fees for the RCC Trial. Salary, benefits and other expenses allocated to CRLX101 increased $0.6 million in 2014 compared to the prior year to support CRLX101 development and clinical trials.

For the year ended December 31, 2014, costs associated with the CRLX301 program were $2.4 million compared to $2.3 million for the year ended December 31, 2013, an increase of $0.1 million, or 6%. The increase in CRLX301 program expense was primarily due to costs associated with the Phase 1 clinical trial that we initiated in December 2014. CRLX301 clinical trial expenses increased by $0.3 million in 2014 compared to the prior year. The increase was due to CRO and laboratory costs associated with initiating our Phase 1 clinical trial of CRLX301 including costs associated with setting up clinical sites and laboratories. Salary and benefits expenses allocated to CRLX301 increased $0.4 million in 2014 compared to the prior year. The increased CRLX301 expenses were partially offset by a $0.3 million decrease in research costs and a $0.3 million decrease in chemistry manufacturing and controls development activities as CRLX301 transitioned into clinical stage development.

Expenses associated with our Dynamic Tumor Targeting Platform decreased $0.8 million in 2014 as compared to 2013, mainly as a result of reduced staff in new discovery research as we continue to shift our emphasis to the development of our existing product candidates.

General and administrative. General and administrative expense for the year ended December 31, 2014 was $8.6 million compared to $6.2 million for the year ended December 31, 2013, an increase of $2.4 million, or 39%. The increase was primarily attributable to the incremental costs of being a public company, including an increase of $1.1 million for board of director fees, insurance for directors and officers, audit and tax fees, and corporate communication and printer fees. Salary and benefits expense increased $0.4 million in 2014 compared to the prior year reflecting additional resources in finance and accounting, legal and corporate communications, along with an increase in stock-based compensation expense. Professional and recruiting fees increased by $0.5 million in 2014 compared to 2013, primarily reflecting increased recruiting and placement fees. Other consulting costs also increased $0.4 million year over year. These increases in general and administrative costs were partially offset by a decrease in legal fees of $0.4 million.

Other expense, net. Other expense, net for the year ended December 31, 2014 was $3.1 million compared to $1.3 million for the year ended December 31, 2013, an increase of $1.8 million. The increase in net other expense primarily resulted from a loss of $2.5 million incurred on the conversion of convertible debt to common stock. The increase was offset by a decrease of $0.3 million due to a decrease in the value of the preferred stock warrant liability and a decrease in interest expense of $0.4 million.

Comparison of Years Ended December 31, 2013 and 2012

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

	Years Ended December 31,		Change	
	2013	2012	Dollar	%
Revenue	$ 6	$ 625	$ (619)	(99)%
Operating expenses:				
Research and development	9,700	15,807	(6,107)	(39)%
General and administrative	6,166	6,393	(227)	(4)%
Loss from operations	(15,860)	(21,575)	5,715	(26)%
Other income/(expense), net	(1,283)	(526)	(757)	144%
Net loss	$ (17,143)	$ (22,101)	$ 4,958	(22)%

Revenue. Revenue for the year ended December 31, 2013 was $6,000 compared to $0.6 million for the year ended December 31, 2012. We recorded revenue in 2013 and 2012 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, 2013 and 2012, together with the change in spending by program in dollars and as a percentage (in thousands, except percentages):

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

Research and development expense for the year ended December 31, 2013 was $9.7 million compared to $15.8 million for the year ended December 31, 2012, 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 our Phase 2 clinical trial of CRLX101 as monotherapy in patients with NSCLC, 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 enabling studies and process development, early in 2013. Expenses associated with our Dynamic

Tumor Targeting 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 decrease in overhead expense 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, 2013 was $6.2 million compared to $6.4 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, 2013 was $1.3 million compared to $0.5 million net expense for the year ended December 31, 2012, an increase of net other expense of $0.8 million. The increase in net other expense primarily resulted from $0.9 million increase in recorded interest expense on our borrowings under the Lighthouse Loan Agreement. 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 of other income for the year ended December 31, 2012.

Liquidity and Capital Resources

From our incorporation through December 31, 2014, we have raised an aggregate of $171.4 million to fund our operations, of which $84.2 million was from the sale of preferred stock in private placements, $59.9 million was from our IPO, $17.3 million was from the sale of convertible promissory notes, and $10.0 million was from borrowings under the Lighthouse Loan Agreement. As of December 31, 2014, we had cash and cash equivalents of approximately $51.2 million.

Indebtedness

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

The Hercules Loan Agreement provides for up to three separate tranches of borrowings, the first of which was funded in the amount of $15.0 million on January 8, 2015. We may draw the second tranche of up to $5.0 million, subject to the satisfaction of customary funding conditions, on or prior to December 15, 2015, provided that we meet certain clinical milestones specified in the Hercules Loan Agreement. We may draw the third tranche of up to $6.0 million at no less than $3.0 million per draw and subject to the satisfaction of customary funding conditions, on or after September 30, 2015 but before December 15, 2015, provided that between January 8, 2015 and December 15, 2015, we have received net cash proceeds of at least $40.0 million from our issuance and sale of equity securities and/or upfront cash payments from one or more strategic corporate partnerships.

Our indebtedness under the Hercules Loan Agreement will mature on July 1, 2018. Each advance under the Hercules Loan Agreement accrues interest at a floating per annum rate equal to the greater of (i) 7.30% or (ii) the sum of 7.30% plus the prime rate minus 5.75%. The Hercules Loan Agreement provides for interest-only payments on a monthly basis until December 31, 2015. The interest only period may be extended at our option for a three month period if we attain certain clinical milestones specified in the Hercules Loan Agreement, and for an additional three month period if we attain certain clinical milestones and receive net cash proceeds of at least $30.0 million from the issuance and sale of our equity securities and/or upfront cash payments from one or more strategic corporate partnerships. Thereafter, amortization payments will be payable monthly in equal installments of principal and interest to fully amortize the outstanding principal over the remaining term of the loan, subject to recalculation upon a change in the prime rate. We may prepay the indebtedness under the Hercules Loan Agreement in whole or in part upon seven business days' prior written notice to Hercules. Any such prepayment is subject to a prepayment charge of (i) 3.0% if such prepayment occurs on or before January 8, 2016, (ii) 2.0% if such prepayment occurs after January 8, 2016, but on or before January 8, 2017, and (iii) 1.0% if such prepayment occurs after January 8, 2017. Amounts outstanding during an event of default are payable upon Hercules' demand and shall accrue interest at an additional rate of 5.0% per annum of the past due amount outstanding. At the end of the loan term (whether at maturity, by prepayment in full or otherwise), we shall make a final payment to Hercules in the amount of 6.70% of the aggregate original principal amount advanced by Hercules.

The Hercules Loan Agreement is secured by substantially all of our assets other than our intellectual property. We have also granted Hercules a negative pledge with respect to our intellectual property, which, among other things, prohibits us from selling, transferring, assigning, mortgaging, pledging, leasing, granting a security interest in or otherwise encumbering our intellectual property. The Hercules Loan Agreement includes restrictive covenants that may restrict our ability to obtain further debt or equity financing.

Lighthouse Loan Agreement. In 2011, we entered into the Lighthouse Loan Agreement, which permitted us to borrow up to an aggregate principal amount of $10.0 million. We borrowed $5.0 million in March 2012 and an additional $5.0 million in August 2012. Interest accrued under the Lighthouse Loan Agreement at an annual rate of 8.25%. As of December 31, 2014, there was $3.3 million

in aggregate principal amount outstanding under the Lighthouse Loan Agreement. We repaid in full our outstanding indebtedness under the Lighthouse Loan Agreement on January 8, 2015.

Convertible Notes. In 2014, we issued and sold 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 accrued interest at an annual rate of 7%. In connection with the completion of our IPO on April 15, 2014, all principal and accrued interest under our 2014 Convertible Notes converted into an aggregate of 1,582,931 shares of our common stock, at 77.5% of the IPO price, or $5.43 per share.

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 accrued interest at an annual rate of 7%. In connection with the completion of our IPO on April 15, 2014, all principal and accrued interest under our 2013 Convertible Notes converted into an aggregate of 1,319,302 shares of our common stock, at the IPO price of $7.00 per share.

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 trial costs, legal and other regulatory expenses and general overhead costs.

We believe that our cash and cash equivalents as of December 31, 2014, together with the net proceeds we received from Hercules on January 8, 2015, will enable us to fund our operating expenses, debt service and capital expenditure requirements into the third quarter of 2016. 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. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and revenue from collaboration arrangements. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or drug candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

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

	Years Ended December 31,		
	2014	2013	2012
Net cash used in operating activities	$ (19,061)	$ (16,614)	$ (21,005)
Net cash used in investing activities	(185)	(7)	(180)
Net cash provided by financing activities	64,932	5,402	22,547
Net increase (decrease) in cash and cash equivalents	$ 45,686	$ (11,219)	$ 1,362

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 $19.1 million for the year ended December 31, 2014, compared with $16.6 million for the year ended December 31, 2013, an increase of $2.5 million. The increase in cash used in operating activities resulted from an increase in operating expenses of $4.5 million, partially offset by changes in the components of working capital of $1.7 million and a decrease in interest payments on our debt facility with Lighthouse Capital of $0.3 million.

Net cash used in operating activities was $16.6 million for the year ended December 31, 2013 compared with $21.0 million for the year ended December 31, 2012, a decrease of $4.4 million. The decrease primarily resulted from a $6.3 million decrease in operating expenses, which was partially offset by a $0.7 million increase in interest payments on our debt facility with Lighthouse Capital, $0.6 million in revenue from material transfer agreements 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 reflects purchases of property and equipment of $225,000 for the year ended December 31, 2014 compared to $7,000 for the year ended December 31, 2013, an increase of $218,000. The increase is attributable to purchases of laboratory, office and computer equipment of $173,000 and furniture, fixtures and leasehold improvements of $52,000 in the year ended December 31, 2014, compared to laboratory equipment purchases of $7,000 in the year ended December 31, 2013. The increase for the year ended December 31, 2014 was partially offset by proceeds of $40,000 from the sale of property and equipment.

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

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $65.0 million for the year ended December 31, 2014 compared with $5.4 million for the year ended December 31, 2013. For the year ended December 31, 2014, we raised net proceeds of $59.9 million from our IPO and $8.3 million through the sale of convertible promissory notes compared to raising $8.8 million through the sale of convertible promissory notes for the year ended December 31, 2013. We repaid indebtedness under the Loan Agreement with Lighthouse Capital in the amount of $3.3 million for the year ended December 31, 2014 compared to repayments of $3.1 million for the year ended December 31, 2013. We received $0.1 million of proceeds from the exercise of common stock options for the year ended December 31, 2014 compared to $35,000 for the year ended December 31, 2013.

Net cash provided by financing activities was $5.4 million for the year ended December 31, 2013 compared to $22.5 million during the year ended December 31, 2012. During the year ended December 31, 2013, we sold $8.8 million in convertible promissory notes, repaid indebtedness under the Lighthouse Loan Agreement in the amount of $3.1 million and 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 the Lighthouse Loan Agreement and repaid indebtedness under the Lighthouse Loan Agreement in the amount of $0.4 million.

Contractual Obligations and Contingent Liabilities

The following summarizes our significant contractual obligations as of December 31, 2014 (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)	$ 1,114	$ 954	$ 160		—
Debt Obligations(2)	$ 4,036	$ 4,036	—	—	—

(1) Represents minimum future lease payments under our non-cancellable operating lease. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes. On July 11, 2014, we signed a lease amendment to expand our leased premises at 840 Memorial Drive, Cambridge, Massachusetts, by approximately 8,628 rentable square feet. The amendment became effective on July 15, 2014, and the lease expires on February 29, 2016. For the year ended December 31, 2014 total base rent for all of our rented space at 840 Memorial Drive amounted to approximately $737,000.

(2) Consists of payment obligations for principal and interest to Lighthouse Capital under the Lighthouse Loan Agreement. As of December 31, 2014, we had $3.2 million in outstanding borrowings under the debt facility, bearing interest at 8.25% with a one-time final payment of 6% of the original principal amount of $10.0 million 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 paid to Calando in January 2015 a $250,000 clinical development milestone to Calando following the initiation of our Phase 1 clinical trial of CRLX301 in December 2014. In addition, under the Platform Agreement, we will be required to pay to Calando: (1) additional milestone payments in an aggregate amount of up to $17.8 million to Calando upon the achievement of certain regulatory and commercial milestones, (2) 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 (3) a percentage, in the low-double digits, of any licensing or sublicensing income we receive from our license or sublicense of CRLX301.

The contractual obligations table does not include the $15.0 million borrowing under the Hercules Loan Agreement entered into on January 8, 2015, and potential payments we may be required to make under manufacturing and CRO agreements as the timing of when these payments will actually be made is uncertain and the payments are contingent upon the initiation and completion of future activities.

Off-Balance Sheet Arrangements

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

Recent Accounting Pronouncements

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

In June 2014, the FASB issued ASU No. 2014-10, *Development Stage Entities: Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation*. This accounting standard eliminates all incremental financial reporting requirements from generally accepted accounting principles in the United States for development stage entities. This ASU is effective on a prospective basis for annual and interim reporting periods beginning on or

after December 15, 2014, with early adoption permitted. We elected to early adopt the ASU starting with our June 30, 2014 financial statements and, accordingly, have not included inception to date information in our financial statements appearing elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of December 31, 2014, we had cash and cash equivalents of approximately $51.2 million, consisting primarily of investments in money market funds and certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. 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.

Item 8. Financial Statements and Supplementary Data

CERULEAN PHARMA INC.

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. and subsidiary (the "Company") as of December 31, 2014 and 2013, and the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2014. 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, 2014 and 2013, and the results of their consolidated operations and their cash flows for each of the three years in the period ended December 31, 2014, in conformity with accounting principles generally accepted in the United States of America.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 19, 2015

CERULEAN PHARMA INC.

CONSOLIDATED BALANCE SHEETS (In thousands, except share data and par value)

	December 31,	
	2014	2013
ASSETS		
Current assets:		
Cash and cash equivalents	$ 51,174	$ 5,488
Accounts receivable, prepaid expenses, and other current assets	1,662	959
Total current assets	52,836	6,447
Property and equipment — Net	342	245
Other assets	215	135
Total	$ 53,393	$ 6,827
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Current portion of loan payable	$ 3,124	$ 3,134
Convertible promissory notes payable to shareholders	—	8,824
Accounts payable	1,255	914
Accrued expenses	3,648	2,274
Other liabilities	34	—
Total current liabilities	8,061	15,146
Long-term liabilities:		
Loan payable — net of current portion	—	3,124
Preferred stock warrant liability	—	928
Noncurrent accrued interest	—	391
Other	7	12
Total long-term liabilities	7	4,455
Redeemable convertible preferred stock (Note 8)	—	81,525
Commitments (Note 13)		
Stockholders' equity (deficit):		
Preferred stock, $0.01 par value; 5,000,000 shares authorized, no shares issued or outstanding	—	—
Common stock, $0.0001 par value; 120,000,000 shares authorized, 20,125,049 and 785,531 shares issued and outstanding at December 31, 2014 and 2013, respectively	2	—
Additional paid-in capital	167,104	4,140
Accumulated deficit	(121,781)	(98,439)
Total stockholders' equity (deficit)	45,325	(94,299)
Total	$ 53,393	$ 6,827

See notes to consolidated financial statements.

CERULEAN PHARMA INC.

CONSOLIDATED STATEMENTS OF OPERATIONS (In thousands, except per share and share data)

	Years Ended December 31,		
	2014	2013	2012
Revenue	$ 80	$ 6	$ 625
Operating expenses:			
Research and development	11,772	9,700	15,807
General and administrative	8,587	6,166	6,393
Total operating expenses	20,359	15,866	22,200
Other income (expense):			
Interest income	9	2	2
Interest expense	(1,083)	(1,487)	(567)
Loss on extinguishment of debt	(2,493)	—	—
Decrease in value of preferred stock warrant liability	504	202	39
Total other income (expense) — net	(3,063)	(1,283)	(526)
Net loss	(23,342)	(17,143)	(22,101)
Accretion of redeemable convertible preferred stock	—	—	(73)
Net loss attributable to common stockholders	$ (23,342)	$ (17,143)	$ (22,174)
Net loss per share attributable to common stockholders:			
Basic and diluted	$ (1.60)	$ (25.05)	$ (36.39)
Weighted-average common shares outstanding:			
Basic and diluted	14,548,516	684,330	609,344

See notes to consolidated financial statements.

CERULEAN PHARMA INC.

CONSOLIDATED STATEMENT OF REDEEMABLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share data and par value)

	Redeemable Convertible Preferred Stock $0.01 Par Value		Common Stock $0.0001 Par Value		Additional Paid-In	Accumulated	
	Shares	Amount	Shares	Amount	Capital	Deficit	Total
BALANCE — December 31, 2011	71,374,896	$ 70,751	609,041	$ —	$ 798	$ (59,195)	$ (58,397)
Exercise of stock options			904		3		3
Sale of Series D Convertible Preferred Stock at $0.83 per share, net of issuance costs of $73	15,662,650	12,927					
Stock-based compensation					529		529
Accretion of issuance costs to redemption value		73			(73)		(73)
Net loss						(22,101)	(22,101)
BALANCE — December 31, 2012	87,037,546	83,751	609,945	—	1,257	(81,296)	(80,039)
Exercise of stock options			8,911		35		35
Stock-based compensation					622		622
Conversion of preferred stock into common stock at $14.51 to $39.21 per share	(1,830,190)	(2,226)	166,675		2,226		2,226
Net loss						(17,143)	(17,143)
BALANCE — December 31, 2013	85,207,356	81,525	785,531	—	4,140	(98,439)	(94,299)
Exercise of stock options			41,566		140		140
Stock-based compensation					885		885
Issuance of common stock from initial public offering, net of underwriting fees and issuance costs of $7,126			9,569,715	1	59,861		59,862
Conversion of convertible preferred stock into common stock	(85,207,356)	(81,525)	6,826,004	1	81,525		81,526
Reclassification of warrants in connection with initial public offering					424		424
Conversion of convertible notes, net of issuance costs of $187			2,902,233		20,129		20,129
Net loss						(23,342)	(23,342)
BALANCE — December 31, 2014	—	$ —	20,125,049	$ 2	$ 167,104	$ (121,781)	$ 45,325

See notes to consolidated financial statements.

CERULEAN PHARMA INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS (In thousands)

	Years Ended December 31,		
	2014	2013	2012
Cash flows from operating activities:			
Net loss	$ (23,342)	$ (17,143)	$ (22,101)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	885	622	529
Noncash rent expense	29	(1)	(68)
Change in carrying value of preferred stock warrant liability	(504)	(202)	(39)
Depreciation and amortization	126	197	346
Loss (gain) on disposal of property and equipment	(28)	7	2
Loss on extinguishment of debt	2,493	—	—
Noncash interest expense	416	588	61
Changes in operating assets and liabilities:			
Accounts receivable, prepaid expenses and other current assets	(713)	(229)	(61)
Accounts payable	341	14	(163)
Accrued expenses	1,236	(467)	489
Net cash used in operating activities	(19,061)	(16,614)	(21,005)
Cash flows from investing activities:			
Purchases of property and equipment	(225)	(7)	(180)
Proceeds from sale of property and equipment	40	—	-
Net cash used in investing activities	(185)	(7)	(180)
Cash flows from financing activities:			
Proceeds from sale of common stock	140	35	3
Proceeds from issuance of convertible promissory notes	8,500	8,824	-
Proceeds from initial public offering, net	59,862		
Proceeds from loans payable	—	—	10,000
Payments on capital lease	—	—	(3)
Payments on loans payable	(3,348)	(3,084)	(376)
Cash paid for debt issuance costs	(222)	(373)	(4)
Proceeds from sale of redeemable convertible preferred stock, net of issuance costs	—	—	12,927
Net cash provided by financing activities	64,932	5,402	22,547
Net increase (decrease) in cash and cash equivalents	45,686	(11,219)	1,362
Cash and cash equivalents — Beginning of year	5,488	16,707	15,345
Cash and cash equivalents — End of year	$ 51,174	$ 5,488	$ 16,707
Supplemental disclosures of noncash investing and financing activities:			
Conversion of redeemable convertible preferred stock into common stock	$ 81,526	$ 2,226	$ —
Conversion of convertible notes and accrued interest into common stock, net	$ 20,129	$ —	$ —
Reclassification of warrants to additional paid-in capital	$ 424	$ —	$ —
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ —	$ 73
Fair value of preferred stock warrants issued in connection with debt	$ —	$ —	$ 360
Supplemental cash flow information — Interest paid	$ 400	$ 664	$ 507

See notes to consolidated financial statements.

CERULEAN PHARMA INC.

NOTES TO 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. In 2013, the Company formed a wholly-owned subsidiary, Cerulean Pharma Australia Pty Ltd as an Australian-based proprietary limited company, to perform clinical activities in Australia. To date, operations of the Australia subsidiary have been immaterial.

The Company's operations to date have consisted primarily of raising capital, product research and development, and initial market development. Accordingly, the Company is considered to be in the development stage at December 31, 2014.

The Company has not generated any revenue related to its primary business purpose to date and is subject to a number of risks similar to those of other development stage life science companies, including dependence on key individuals, competition from other companies, the need for development of commercially viable products, and the need to obtain adequate additional financing to fund the development of its product candidates. The Company is also subject to a number of risks similar to other companies in the industry, including rapid technological change, regulatory approval of products, uncertainty of market acceptance of products, competition from substitute products and larger companies, the need to obtain additional financing, compliance with government regulations, protection of proprietary technology, dependence on third parties, product liability and dependence on key individuals.

The Company has an accumulated deficit of $121.8 million at December 31, 2014. The Company has financed its operations primarily through private placements of its preferred stock, proceeds from borrowings, and an initial public offering completed in 2014. The Company has not completed development of any product candidate and has devoted substantially all of its financial resources and efforts to research and development, including preclinical and clinical development. The Company expects to continue to incur significant expenses and increasing operating losses for at least several years.

Initial Public Offering — On April 15, 2014, the Company completed the sale of 8,500,000 shares of its common stock in its initial public offering (the "IPO"), at a price to the public of $7.00 per share. On May 7, 2014, the Company completed the sale of an additional 1,069,715 shares of common stock at a price to the public of $7.00 per share under a partial exercise by the underwriters of their option to purchase additional shares of common stock. The sale of shares to the public resulted in net proceeds of $59.9 million after deducting underwriting discounts and commissions and offering expenses payable by the Company.

In preparation for the IPO, the Company's board of directors and stockholders approved a 1-for-14.5074 reverse stock split of the Company's common stock effective March 31, 2014. All share and per share amounts in the consolidated financial statements contained herein and notes thereto have been retroactively adjusted, where necessary, to give effect to this reverse stock split. In connection with the closing of the IPO, all of the Company's outstanding redeemable convertible preferred stock and convertible notes automatically converted into shares of common stock as of April 15, 2014, resulting in the issuance by the Company of an additional 9,728,237 shares of common stock. The significant increase in shares outstanding in April 2014 is expected to impact the year-over-year comparability of the Company's net loss per share calculations in future periods.

In connection with the completion of the IPO on April 15, 2014, the Company's outstanding warrants to purchase 1,857,226 shares of the Company's preferred stock automatically converted into warrants to purchase an aggregate of 128,663 shares of the Company's common stock and, as a result, the Company reclassified the warrant liability to additional paid-in capital.

2. SIGNIFICANT ACCOUNTING POLICIES

Use of Estimates — The preparation of 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 the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period.

On an ongoing basis, the Company's management evaluates its estimates, including estimates related to clinical trial accruals, stock-based compensation expense, and reported amounts of revenues and expenses during the reported period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Although the Company regularly assesses these estimates, actual results could differ from those estimates. Changes in estimates are recorded in the period in which they become known.

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.

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; however, the Company operates in two geographic regions: United States (Cambridge, MA) and Australia (Sydney, NSW). There is no revenue generated or long-lived assets located within the Australian location.

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, 2014 and 2013, the Company has restricted cash of $117,000 representing a letter of credit for the Company's facility lease that is scheduled to expire in February 2016. The letter of credit is secured by certificates of deposit that renew monthly. The restricted cash is included within other assets in the balance sheet.

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	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, 2014 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.

Comprehensive Loss — Comprehensive loss consists of net loss and changes in equity during a period from transactions and other equity and circumstances generated from non-owner sources. The Company had no items of comprehensive loss, other than its net loss, for each of the periods presented.

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. All of the

Company's warrants to purchase preferred stock were converted to warrants to purchase common stock upon the Company's IPO in April 2014. Accordingly, the preferred stock warrant liability was reclassified to additional paid-in capital.

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. All of the Company's redeemable convertible preferred stock was automatically converted to common stock in connection with the Company's IPO in April 2014.

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. The Company issued performance based grants where the vesting of the grant is tied to certain milestone performance and in these cases, the compensation is recognized as expense when the probability of the milestone is met.

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"). 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 and warrants 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, 2014 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.

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

In June 2014, the FASB issued ASU No. 2014-10, "*Development Stage Entities: Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation*." This accounting standard eliminates all incremental financial reporting requirements from U.S. GAAP for development stage entities, thereby

improving financial reporting by reducing the cost and complexity associated with providing such information. The Company will no longer be required to present inception-to-date information. This ASU is effective on a prospective basis for annual and interim reporting periods beginning on or after December 15, 2014, with early adoption permitted. The Company elected to early adopt the ASU starting with its June 30, 2014 financial statements and, accordingly, has not included inception to date information it the accompanying financial statements.

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 (in thousands, except share data and per share data):

	Years Ended December 31,		
	2014	2013	2012
Net loss	$ (23,342)	$ (17,143)	$ (22,101)
Accretion of preferred stock issuance costs to redemption value	—	—	(73)
Net loss attributable to common stockholders — basic and diluted	$ (23,342)	$ (17,143)	$ (22,174)
Weighted-average number of common shares — basic and diluted	14,548,516	684,330	609,344
Net loss per share attributable to common stockholders — basic and diluted	$ (1.60)	$ (25.05)	$ (36.39)

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 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,		
	2014	2013	2012
Options to purchase common stock	2,126,176	1,062,694	1,046,178
Warrants to purchase redeemable convertible preferred stock	—	128,663	128,663
Warrants to purchase common stock	128,663	—	—
Redeemable convertible preferred stock	—	6,826,004	6,992,694
Convertible notes payable	—	754,785	—

4. PROPERTY AND EQUIPMENT

Property and equipment consist of the following (in thousands):

	As of December 31,	
	2014	2013
Laboratory equipment	$ 1,163	$ 1,246
Computer equipment	260	183
Office furniture and equipment	292	257
Leasehold improvements	117	91
	1,832	1,777
Less accumulated depreciation and amortization	(1,490)	(1,532)
Property and equipment, net	$ 342	$ 245

Depreciation and amortization expense for the years ended December 31, 2014, 2013 and 2012 was $126,000, $197,000 and $346,000, respectively.

5. ACCRUED EXPENSES

Accrued expenses consist of the following (in thousands):

	As of December 31,	
	2014	2013
Accrued expenses	$ 663	$ 379
Accrued clinical trial costs	848	610
Accrued contract manufacturing expenses	580	433
Accrued compensation and benefits	983	618
Accrued interest	574	234
Total accrued expenses	$ 3,648	$ 2,274

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. 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. The Company determined the fair value of the warrants at the end of each subsequent reporting period using the Black-Scholes option-pricing model (see Note 11) until their conversion to warrants to purchase 60,532 shares of common stock upon the IPO in April 2014.

In August 2013, the Company issued convertible promissory notes in the amount of $8,824,000 to existing investors, with a stated interest rate of 7%. Outstanding principal and unpaid accrued interest due under the notes were automatically converted into shares of the Company's common stock upon the closing of the Company's IPO in April 2014.

In February and March 2014, the Company issued convertible promissory notes in the aggregate amount of $6,000,000 to existing investors and a convertible promissory note in the amount of $2,500,000 to a new investor. All the notes had a stated interest rate of 7%. Outstanding principal and unpaid accrued interest due under the notes were automatically converted into shares of the Company's common stock upon the closing of the Company's IPO in April 2014, at a conversion price equal to 77.5% of the IPO price. The Company recorded a loss on the extinguishment of the notes of $2,493,000 in April 2014, equal to the difference between the fair value of the shares into which the notes converted and the carrying amount of the notes upon the closing of the Company's IPO.

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. 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. The Company determined the fair value of the warrants at the end of each subsequent reporting period using the Black-Scholes option pricing model (see Note 11) until their conversion to common stock warrants to purchase 1,695 shares of common stock upon the completion of the IPO in April 2014.

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. 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 was 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 amount accrued as of December 31, 2014 was $574,000 and is included in accrued expense in the accompanying balance sheet. As of December 31, 2013 the amount accrued was $391,000, and was included as non-current accrued interest expense in the accompanying balance sheet. The minimum future principal payments are as follows (in thousands):

Year Ending December 31,	
2015	$ 3,321
Unamortized discount relating to warrants	(197)
Total	3,124
Less current portion	(3,124)
Long-term portion	$ -

In January 2015, the Company repaid in full the amount outstanding under the Lighthouse Capital loan with the proceeds from a new loan (see Note 18).

In connection with the loan and security agreement with Lighthouse Capital, the Company issued the lender a warrant to purchase a maximum of 66,436 shares of the Company's Series D Preferred Stock, at an exercise price of $12.04 per share. The warrant was immediately exercisable for 29,067 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, 2014 and 2013, 66,436 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 loan and is being amortized to interest expense using the effective interest method over the 36-month repayment term.

The Company determined the fair value of the warrant at the end of each subsequent reporting period using the Black-Scholes option pricing model (see Note 11) until their conversion to warrants to purchase 66,436 shares of common stock upon the completion of the IPO in April 2014.

8. REDEEMABLE CONVERTIBLE PREFERRED STOCK

In connection with the closing of the IPO in April 2014, all of the Company's outstanding convertible preferred stock automatically converted to common stock resulting in an additional 6,826,004 shares of common stock of the Company becoming outstanding.

As of December 31, 2013, preferred stock consisted of the following (in thousands, except share data):

	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	$ 2,000
Series A	9,307,692	May 2007	9,307,692	12,100	12,100
Series B	4,077,500	December 2007	3,562,500	7,125	7,125
Series B-1	5,000,000	July 2009	4,842,500	9,685	9,685
Series C	33,310,787	November 2010 and June 2011	31,836,392	23,559	23,094
Series D	34,698,793	December 2011 and November 2012	33,158,272	27,521	27,521
	88,894,772		85,207,356	$ 81,990	$ 81,525

9. STOCKHOLDERS' EQUITY (DEFICIT)

Common Stock — As discussed in Note 1, during 2014 the Company issued 19,297,952 shares of common stock in connection with its IPO, the conversion of preferred stock and convertible notes into common stock, and the partial exercise of the underwriters' overallotment option in the IPO.

Reserved Shares of Common Stock — The Company has reserved the following number of shares of common stock at December 31, 2014 and 2013:

	As of December 31,	
	2014	2013
Redeemable convertible preferred stock	—	6,954,691
Warrants to purchase common stock	128,663	—
Common stock options	3,561,104	1,201,770
Total	3,689,767	8,156,461

10. STOCK OPTION PLANS

2007 Stock Incentive Plan – The Company's 2007 Incentive Stock Plan, or the 2007 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 1,275,211 shares of the Company's common stock, as amended in January 2014. 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 2007 Plan. Effective with the IPO, no additional grants will be issued from the 2007 Plan and all shares available for grant under the 2007 Plan were transferred to the 2014 Plan. Accordingly, at December 31, 2014, there were no shares available for future grant under the 2007 Plan. At December 31, 2013, there were 139,076 shares available for future grant under the 2007 Plan.

Prior to the IPO, in determining the exercise prices for options granted, the Company's board of directors considered the fair value of the common stock as of the measurement date. The fair value of the common stock was 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.

2014 Stock Incentive Plan – In March 2014, the Company's board of directors adopted and its stockholders approved the 2014 Stock Incentive Plan, or the 2014 Plan, which became effective upon the closing of the IPO. 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. As of December 31, 2014, there were 1,434,928 shares available for future grant under the 2014 Plan.

A summary of stock option activity for employee and nonemployee awards under the 2007 Plan and the 2014 Plan during the year ended December 31, 2014 is presented below:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value
Outstanding — January 1, 2014	1,062,694	$ 3.98	7.2	$ 7,028
Granted	1,138,170	5.99		
Exercised	(41,566)	3.36		
Forfeited	(33,122)	4.85		
Outstanding — December 31, 2014	2,126,176	$ 4.97	6.7	$ 2,701
Options expected to vest — December 31, 2014	859,690	$ 5.46	9.2	$ 1,105
Options exercisable — December 31, 2014	786,623	$ 4.41	3.9	$ 1,541

The total intrinsic value of stock options exercised in the years ended December 31, 2014, 2013 and 2012 was $161,000, $15,000, and $0, respectively.

The weighted-average per share grant date fair value of options granted during 2014, 2013 and 2012 was $3.33, $2.90, and $2.61, respectively.

The Company has recorded stock-based compensation expense of $885,000, $622,000 and $529,000 during the years ended December 31, 2014, 2013 and 2012, respectively, which is based on the number of awards ultimately expected to vest. As of December 31, 2014, there was $2.2 million of unrecognized compensation cost related to unvested stock-based compensation arrangements granted under the 2007 Plan and the 2014 Plan. The compensation is expected to be recognized over a weighted-average period of 3.02 years at December 31, 2014.

Stock-based compensation expense recorded as research and development and general and administrative expenses is as follows (in thousands):

	As of December 31,		
	2014	2013	2012
Research and development	$ 317	$ 284	$ 187
General and administrative	568	338	342
Total	$ 885	$ 622	$ 529

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.

The assumptions used in the Black-Scholes option-pricing model for stock options granted to employees during the years ended December 31, 2014, 2013 and 2012 are as follows:

	December 31,		
	2014	2013	2012
Expected life	6 years	6 years	6 years
Risk-free interest rate	1.71%-2.00%	1.09%-1.92%	0.83%-1.12%
Expected volatility	54%-60%	59%-79%	77%-79%
Expected dividend rate	—%	—%	—%

The Company recorded stock-based compensation expense related to nonemployee awards of $56,000, $85,000 and $39,000 for the years ended December 31, 2014, 2013 and 2012, 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 the fair value of these awards for the years ended December 31, 2014, 2013 and 2012 were as follows:

	December 31,		
	2014	2013	2012
Expected life	8 years	7 years	6 years
Risk-free interest rate	1.86%-2.53%	1.11%-2.86%	0.99%-2.05%
Expected volatility	56%-62%	56%-79%	76%-79%
Expected dividend rate	—%	—%	—%

The Company did not grant any nonemployee stock option grants in 2014 or in 2013, except for a performance award grant in 2013 to the Company's board chairman for non-board related services. During the year ended December 31, 2014, the board of directors changed the vesting conditions of this award from performance-based vesting to time-based vesting and reduced the total number of shares subject to the stock option. As a result, the 16,000 shares subject to this stock option now vest over three years, with the first third vesting on March 26, 2014. The change in vesting condition was accounted for as a modification of this stock option, which had an immaterial impact on the Company's financial statements.

In 2013 and 2012, the Company granted to the Company's Chief Executive Officer ("CEO") options to purchase up to 53,489 and 56,053 shares of common stock, respectively. The vesting of these awards was contingent upon either (i) a change of control at a minimum price per share or (ii) the registration of the Company's common stock under the Securities Exchange Act of 1934 and the stock being quoted, listed or traded on an over-the-counter market or national securities exchange at a certain price per share. The CEO resigned in October 2014 and although the Company completed its IPO in April 2014, the minimum price per share required was never achieved therefore these awards will not vest. Also in 2012, the Company granted options to purchase 60,934 common shares to a second Company officer that will vest upon the achievement of business milestones as defined within the stock option agreement. These awards have not vested as of December 31, 2014. Compensation expense for the awards will be recorded if and when the awards are determined to be probable.

2014 Employee Stock Purchase Plan – In March 2014, the Company's board of directors adopted and its stockholders approved the 2014 Employee Stock Purchase Plan (the "2014 ESPP"), which became effective upon the closing of the IPO. The 2014 ESPP will be administered by the Company's board of directors or by a committee appointed by the Company's board of directors. The 2014 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate 500,000 of shares of the Company's common stock. The number of shares of the Company's 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 January 1, 2024, in an amount equal to the least of (i) 600,000 shares of the Company's common stock, (ii) 1% of the total number of shares of the Company's common stock outstanding on the first day of the applicable year, or (iii) an amount determined by the Company's board of directors. The Company did not offer shares to its employees under the 2014 ESPP during the year ended December 31, 2014.

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. If recorded at fair value, Level 2 measurements, as defined below, would have been used to estimate the fair value. Included in cash and cash equivalents as of December 31, 2014 and 2013, are money market fund investments of $50,541,000 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, 2014 and 2013, is as follows (in thousands):

		Fair Value Measurements Using		
	Carrying Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
December 31, 2014				
Money market funds	$ 50,541	$ —	$ 50,541	$ —
December 31, 2013				
Money market funds	$ 5,233	$ —	$ 5,233	$ —
Preferred stock warrant liability	928	—	—	928

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, 2014 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 — December 31, 2012	$ 7	$ 500	$ 623	$ 1,130
Decrease in fair value recorded in other income	(3)	(114)	(85)	(202)
Balance — December 31, 2013	4	386	538	928
Fair value reclassified to additional paid-in capital in connection with the IPO on April 15, 2014	(4)	(386)	(538)	(928)
Balance — December 31, 2014	$ -	$ -	$ -	$ -

The Company's warrants were valued using the Black-Scholes option-pricing model. The fair values were derived by applying the following assumptions:

	December 31, 2013
Expected life	4-8 years
Risk-free interest rate	2.90%
Expected volatility	64%-84%
Expected dividend rate	—%

The preferred stock warrants were automatically adjusted on the date of the closing of the IPO to provide for the issuance of shares of common stock upon their exercise, and is no longer measured at fair value.

12. INCOME TAXES

Significant components of the Company's deferred taxes at December 31, 2014 and 2013 are as follows:

	2014	2013
Net operating loss carryforwards	$ 29,442	$ 25,696
Research and development credit carryforwards	1,715	1,525
Capitalized costs	3,503	3,067
Capitalized research and development costs	9,938	6,992
Other	422	220
Total deferred tax assets	45,020	37,500
Valuation allowance	(45,020)	(37,500)
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 2014 and 2013 by approximately $7.6 million and $7.1 million, respectively, due to the increase in the deferred tax assets by the same amount.

A reconciliation of income tax expense computed at the statutory federal income tax rate to income taxes as reflected in the financial statements is as follows:

	Years Ended December 31,	
	2014	2013
Federal income tax expense at statutory rate	34.0%	34.0%
State income tax, net of federal benefit	4.5%	5.0%
Permanent differences	(3.7%)	0.2%
Research and development credit	0.8%	1.4%
Stock compensation	(0.9%)	(1.1%)
Expiration of state net operating loss	(1.7%)	(4.2%)
Other	(0.8%)	0.2%
Change in valuation allowance	(32.2%)	(35.5%)
Effective income tax rate	0.0%	0.0%

At December 31, 2014, the Company has approximately $77.3 million of federal and $58.1 million of state net operating loss carryforwards that expire at various dates through 2034. At December 31, 2014, the Company has approximately $1.2 million of federal and $0.8 million of state research and development credit carryforwards that expire at various dates through 2034 for federal credits and 2029 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, the Commonwealth of Massachusetts, and Australia. The tax years 2006 through 2014 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. At December 31, 2014 and 2013, the Company has not identified any significant uncertain tax positions.

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. In June 2012, the Company exercised its renewal option extending the lease through February 2016. On July 11, 2014, the Company signed a lease amendment for additional office space in the same building which expires concurrent with the lease agreement in February 2016. The lease agreement and amendment include base rent escalation over the lease 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 current and long-term liabilities as of December 31, 2014 and 2013 was $41,000 and $12,000, respectively. Rent expense under this lease was $766,000, $598,000 and

$517,000 for the years ended December 31, 2014, 2013 and 2012, 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.

Future minimum lease payments, including the three-year extension, under the non-cancelable operating lease are as follows (in thousands):

Years Ending December 31,	Operating Leases
2015	954
2016	160
Total	$ 1,114

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 to 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, 2014, 2013 and 2012.

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 was required to pay Calando a $250,000 clinical development milestone upon initiation of a Phase 1 clinical trial for CRLX301. 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.

In connection with this agreement, the Company recorded research and development expense of $250,000 for the year ended December 31, 2014 upon initiation of the Phase 1 clinical trial for CRLX301 in December 2014.

In March 2014, Calando entered Chapter 7 bankruptcy in the District of Delaware and, as a result, the intellectual property rights the Company has obtained from Calando are subject to potential risks that may arise in connection with bankruptcy. For instance, while the Company's ability to develop and/or commercialize its current product candidates and its ability to utilize its platform are not dependent on the rights that it licenses from Calando, its license agreements with Calando could be rejected in connection with Calando's bankruptcy, in which case, the Company could, subject to elections and other rights and defenses that may be available to it, lose certain rights granted to it under such licenses. On March 3, 2015, Calando's bankruptcy trustee submitted an application with the bankruptcy court seeking authority to retain a broker to sell Calando's rights in certain assets including its rights in the license agreements with the Company, the Company has reserved its rights with respect to any such sale.

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 $30,000, $25,000, and $10,000 for the years ended December 31, 2014, 2013 and 2012, 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 $163,000, $145,000 and $165,000 to the 401(k) Plan for the years ended December 31, 2014, 2013 and 2012, 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, 2014 and 2013, were $39,000 and $84,000, respectively. On April 1, 2014, the Company sold used equipment to this entity and recorded proceeds from the sale of $30,000. The agreement was terminated on April 1, 2014.

In August 2013 and February 2014, the Company issued convertible promissory notes to existing investors, as described in Notes 6.

In April 2014, these notes were converted into the Company's common stock in connection with the IPO.

In April 2014, the Company converted all outstanding shares of the Company's preferred stock held by existing investors into 6,826,004 shares of the Company's common stock in connection with the IPO.

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 $61,000 and $6,000 for the years ended December 31, 2014 and 2013, respectively, in connection with this material transfer agreement.

In May 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 $19,000 for the year ended December 31, 2014, in connection with this material transfer agreement.

18. SUBSEQUENT EVENTS

On January 8, 2015 (the "Closing Date"), the Company entered into a term loan facility of up to $26.0 million (the "Term Loan") with Hercules Technology Growth Capital, Inc., or Hercules, the proceeds of which were used to repay the Company's existing term loan facility with Lighthouse Capital and for general corporate and working capital purposes.

The Term Loan is governed by a loan and security agreement, dated January 8, 2015, between the Company and Hercules (the "Hercules Loan Agreement"). The Hercules Loan Agreement provides for up to three separate borrowings, the first of which was funded in the amount of $15.0 million on the Closing Date. The second borrowing of up to $5.0 million may be drawn by the Company, subject to the satisfaction of customary funding conditions, on or prior to December 15, 2015, provided that the Company meets certain clinical milestones. The third borrowing of up to $6.0 million (the "Term C Loan Advance") may be drawn, at no less than $3.0 million per draw and subject to the satisfaction of customary funding conditions, on or after September 30, 2015 but before December 15, 2015, provided that between the Closing Date and December 15, 2015, the Company has received net cash proceeds of at least $40.0 million from the issuance and sale by the Company of its equity securities and/or upfront cash payments from one or more strategic corporate partnerships.

The Term Loan will mature on July 1, 2018. Each advance under the Term Loan accrues interest at a floating per annum rate equal to the greater of (i) 7.30% or (ii) the sum of 7.30% plus the prime rate minus 5.75%. The Term Loan provides for interest-only payments on a monthly basis until December 31, 2015. The interest only period may be extended at the Company's option for a three month period if the Company attains certain clinical milestones, and for an additional three month period if the Company attains certain clinical milestones and receives net cash proceeds of at least $30.0 million from the issuance and sale by the Company of its equity securities and/or upfront cash payments from one or more strategic corporate partnerships. Thereafter, amortization payments will be payable monthly in equal installments of principal and interest to fully amortize the outstanding principal over the remaining term of the loan, subject to recalculation upon a change in the prime rate. The Company may prepay the Term Loan in whole or in part

upon seven business days' prior written notice to Hercules. Any such prepayment of the Term Loan is subject to a prepayment charge of (i) 3.0% if such prepayment occurs within twelve months of the Closing Date, (ii) 2.0% if such prepayment occurs after twelve months following the Closing Date but on or prior to twenty-four months following the Closing Date, and (iii) 1.0% thereafter. Amounts outstanding during an event of default are payable upon Hercules' demand and shall accrue interest at an additional rate of 5.0% per annum of the past due amount outstanding. At the end of the loan term (whether at maturity, by prepayment in full or otherwise), the Company shall make a final payment to the lender in the amount of 6.70% of the aggregate original principal amount advanced by the lender.

In connection with the Hercules Loan Agreement, the Company issued to Hercules a warrant to purchase shares of the common stock of the Company at an exercise price of $6.05 per share. The warrant is initially exercisable for 137,521 shares of common stock. On such date (if any) as a Term C Loan Advance is made to the Company, the warrant shall automatically become exercisable for an additional 34,380 shares of common stock. The exercise price and the number of shares are subject to adjustment upon a merger event, reclassification of the shares of Common Stock, subdivision or combination of the shares of common stock or certain dividend payments. The warrant is exercisable until January 8, 2020.

In connection with the Hercules Loan Agreement, the Company entered into a stock purchase agreement with Hercules, whereby Hercules purchased 135,501 shares of common stock from the Company at a price per share of $7.38, which was equal to the closing price of the common stock on The NASDAQ Global Market on January 7, 2015, for an aggregate purchase price of approximately $1.0 million.

19. QUARTERLY FINANCIAL DATA (unaudited)

The following table summarizes the unaudited quarterly financial data for the last two fiscal years:

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

	Year Ended December 31, 2014			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ 47	$ 33	$ —	$ —
Operating expenses:				
Research and development	1,495	2,648	2,928	4,701
General and administrative	1,510	2,029	2,441	2,607
Total operating expenses	3,005	4,677	5,369	7,308
Other income (expense):				
Interest income	1	2	2	4
Interest expense	(461)	(268)	(191)	(163)
Loss on extinguishment of debt	—	(2,493)	—	—
Decrease in value of preferred stock warrant liability	504	—	—	—
Total other income (expense) — net	44	(2,759)	(189)	(159)
Net loss attributable to common stockholders	$ (2,914)	$ (7,403)	$ (5,558)	$ (7,467)
Net loss per share attributable to common stockholders:				
Basic and diluted	$ (3.70)	$ (0.44)	$ (0.28)	$ (0.37)
Weighted-average common shares outstanding:				
Basic and diluted	786,986	16,883,716	20,124,574	20,125,009

	Year Ended December 31, 2013			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ —	$ —	$ —	$ 6
Operating expenses:				
Research and development	3,479	3,195	1,586	1,440
General and administrative	1,972	1,392	1,227	1,575
Total operating expenses	5,451	4,587	2,813	3,015
Other income (expense):				
Interest income	1	—	—	1
Interest expense	(353)	(326)	(378)	(430)
Loss on extinguishment of debt	—	—	—	—
Decrease in value of preferred stock warrant liability	231	20	(7)	(42)
Total other income (expense) — net	(121)	(306)	(385)	(471)
Net loss attributable to common stockholders	$ (5,572)	$ (4,893)	$ (3,198)	$ (3,480)
Net loss per share attributable to common stockholders:				
Basic and diluted	$ (9.09)	$ (7.96)	$ (4.40)	$ (4.45)
Weighted-average common shares outstanding:				
Basic and diluted	612,836	614,662	726,987	782,335

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We have established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934, as amended, or the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and is accumulated and communicated to management, including the principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2014.

Management's Annual Report on Internal Control Over Financial Reporting

This report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2014 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The following table sets forth the name, age and position of each of our executive officers and directors as of March 1, 2015.

Name	Age	Position
Christopher D. T. Guiffre, J.D.	46	Chief Operating Officer
Edward G. Garmey, M.D.	47	Senior Vice President and Chief Medical Officer
Karen L. Roberts	58	Senior Vice President, Finance and Administration
Paul A. Friedman, M.D. (4)	72	Executive Chairman of the Board
William H. Rastetter, Ph.D. (1)(3)	66	Lead Independent Director
Alan L. Crane	51	Director
Steven E. Hall, Ph.D. (1)(2)	60	Director
Susan L. Kelley, M.D. (4)	60	Director
William T. McKee (1)(3)	53	Director
David Parkinson, M.D. (4)	64	Director
Ram Sasisekharan, Ph.D.	50	Director
Robert I. Tepper, M.D. (2)	59	Director

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

Christopher D. T. Guiffre, J.D. has served as our Chief Operating Officer since October 2014. He previously served as our Senior Vice President and Chief Business Officer. Prior to that, Mr. Guiffre held a number of senior executive positions at various biopharmaceutical companies, including President and Chief Executive Officer of Alvos Therapeutics, Inc., Chief Business Officer at Hydra Biosciences, Inc. and a senior executive at Cubist Pharmaceuticals, Inc., most recently as Senior Vice President, General Counsel and Secretary. Mr. Guiffre has also held several positions at Renaissance Worldwide, Inc., including Vice President, General Counsel and Clerk. Prior to that, he was an Associate at Bingham, Dana & Gould LLP (now known as Morgan, Lewis & Bockius LLP). Mr. Guiffre received a B.S. from Babson College, a J.D. from Boston College Law School, and an M.B.A. from Boston College Carroll School of Management.

Edward G. Garmey, M.D. has served as our Chief Medical Officer and Senior Vice President 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 and as Clinical Development Liaison. Dr. Garmey previously 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, and he serves on the Board of Visitors of Hearth, a Boston-based non-profit organization dedicated to the elimination of homelessness among the elderly.

Karen L. Roberts has served as our Senior Vice President, Finance and Administration since 2010. Prior to joining Cerulean, 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. Ms. Roberts previously 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. from Salem State College.

Paul A. Friedman, M.D. has served as our Executive Chairman since October 2014 and as a director since January 2014. Previously, he was Chief Executive Officer of Incyte Corporation, a public biotechnology company, where he also served as President. Prior to that, Dr. Friedman was President of DuPont Pharmaceuticals Research Laboratories, a wholly owned subsidiary of DuPont Pharmaceuticals Company (formerly The DuPont Merck Pharmaceutical Company), President of Research and Development of The DuPont Merck Pharmaceutical Company, and 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 company Synta Pharmaceuticals Corp. and private biopharmaceutical company Gliknik, Inc. Dr. Friedman was a director of Bausch & Lomb Incorporated, Sirtris Pharmaceuticals, Inc. and Auxilium

Pharmaceuticals, Inc., until the acquisition of each of these companies. 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.

William H. Rastetter, Ph.D. has served as a director since January 2014 and as our lead independent director since April 2014. He is a Co-Founder of Receptos, Inc., a biopharmaceutical company, where he serves as Director and Chairman of the Board, and previously held the role of Acting Chief Executive Officer. Dr. Rastetter served as a Partner at the venture capital firm of Venrock Associates. 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). He joined Idec Pharmaceuticals 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., Fate Therapeutics Inc. and Receptos, Inc. and as a director of Regulus Therapeutics, Inc. 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. from the Massachusetts Institute of Technology and received his M.A. and Ph.D. 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.

Alan L. Crane is one of our co-founders and has served as a member of our board of directors since 2006. Mr. Crane served as our Chairman from 2009 to 2014. From our founding until 2009, Mr. Crane served as Cerulean's Chief Executive Officer. Currently, he is Partner and Entrepreneur at Polaris Partners and previously served as a Venture Partner at Polaris. Mr. Crane has also served as 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. Mr. Crane serves on the boards of public life sciences company, T2 Biosystems, Inc., and private life sciences companies Arsia Therapeutics, Inc., Visterra, Inc. Seventh Sense Biosystems, Inc., Navitor Pharmaceuticals, Inc., XTuit Pharmaceuticals, Inc., and Vaccinex, Inc. Previously, he served on the boards of Sirtris Pharmaceuticals, Inc. (acquired by GlaxoSmithKline), Adnexus Therapeutics, Inc. (acquired by Bristol Myers Squibb), Hydra Biosciences, Inc. and Ocular Therapeutix, Inc. 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.

Steven E. Hall, Ph.D. has served as a director since 2010. Dr. Hall serves as a general partner at Lilly Ventures, the venture capital arm of Eli Lilly and Company and serves as President and Chief Executive Officer at privately held Esanex, Inc. Prior to joining Lilly Ventures, 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. Dr. Hall has held multiple research management positions, at companies including Eli Lilly, Sphinx Inc., and Bristol-Myers Squib. Dr. Hall is the author of more than 40 papers and 60 patents. Dr. Hall currently sits on the boards of privately held life sciences companies FORMA Therapeutics, Inc., Esanex, Inc., Nimbus Discovery, LLC, Lysosomal Therapeutics, Inc., Numerate, Inc. and Hydra Biosciences, Inc. Dr. Hall received his B.S. from Central Michigan University and his Ph.D. from Massachusetts Institute of Technology. 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.

Susan L. Kelley, M.D. has served as our director since October 2014. Dr. Kelley has been developing drugs in oncology and immunology for over 25 years. She was previously Chief Medical Officer of the Multiple Myeloma Research Consortium and its sister organization, the Multiple Myeloma Research Foundation. Dr. Kelley has held positions of increasing responsibility at Bayer Healthcare Pharmaceuticals and Bayer-Schering Pharma, including Vice President, Global Clinical Development and Therapeutic Area Head – Oncology, where she led the Bayer team responsible for the development and worldwide regulatory approval of Nexavar® (sorafenib), including a renal cell carcinoma indication. She also held positions of increasing responsibility at Bristol-Myers Squibb in Oncology and Immunology drug development. She was a Fellow in Medical Oncology and Clinical Fellow in Medicine at Dana-Farber Cancer Institute, Harvard Medical School, and a Fellow in Medical Oncology and Pharmacology at Yale University School of Medicine, where she also served as a Clinical Assistant Professor of Medicine. Dr. Kelley currently serves as a member of the boards of directors of public oncology-focused biotechnology companies ArQule, Inc. and Alchemia, Pty Ltd. Dr. Kelley received her M.D. from Duke University School of Medicine. We believe that Dr. Kelley is qualified to serve on our board of directors due to her experience in life sciences and clinical development and her experience as a director of other life sciences companies.

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 until EKR was sold to Cornerstone Therapeutics Inc. Prior to that, 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. 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 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. Mr. McKee previously worked at Gramkow & Carnevale, CPA's, an accounting firm, and also worked at Deloitte & Touche. Mr. McKee serves on the board of directors of Agile Therapeutics, Inc., a public specialty biopharmaceutical company, and previously served on the board of Auxilium Pharmaceuticals, Inc. until its acquisition. 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.

David Parkinson, M.D. has served as a director since October 2014. Dr. Parkinson is a venture partner at New Enterprise Associates. Dr. Parkinson previously served as President and Chief Executive Officer of Nodality, a San Francisco-based biotechnology company. Prior to that, Dr. Parkinson was Senior Vice President of Oncology Research and Development at Biogen Idec, Vice President of Oncology Development at Amgen and Vice President of Global Clinical Oncology Development at Novartis. Dr. Parkinson also worked at the National Cancer Institute, serving as Chief of the Investigational Drug Branch and as acting Associate Director of the Cancer Therapy Evaluation Program. He has also held academic positions at the M.D. Anderson Cancer Center, University of Texas and New England Medical Center at Tufts University School of Medicine. Dr. Parkinson is a past Chairman of the Food & Drug Administration Biologics Advisory Committee and is a recipient of the FDA's Cody Medal. He is a past President of the International Society of Biological Therapy, and past editor of the *Journal of Immunotherapy*. He has served a term on the FDA's Science Board, on the Board of Directors of the American Association of Cancer Research and on the National Cancer Policy Forum of the Institute of Medicine. Dr. Parkinson received his M.D. as gold medalist from the University of Toronto Faculty of Medicine, with internal medicine and hematology/oncology training in Montreal at McGill University and in Boston at New England Medical Center. We believe that Dr. Parkinson is qualified to serve on our board of directors due to his experience in life sciences and knowledge of regulatory issues related to drug development.

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 serves as a Professor of Biological Engineering at the Massachusetts Institute of Technology 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. from Bangalore University, his M.S. from Harvard University and his Ph.D. 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 director 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. 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., Dr. Tepper served as President of Research and Development at Millennium Pharmaceuticals, Inc. Before joining Millennium Pharmaceuticals, Inc., 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 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., Jounce Therapeutics, 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. Dr. Tepper holds an A.B. from Princeton University and an M.D. from Harvard Medical School. 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.

Audit committee

Our board of directors has established an audit committee, which operates under a charter that has been approved by our board of directors. The members of our audit committee are Drs. Hall and Rastetter and Mr. McKee. Mr. McKee chairs the audit committee. The audit committee's responsibilities 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 each of these directors is independent within the meaning of Rule 10A-3 under the Securities Exchange Act of 1934, or the Exchange Act. Our board of directors has determined that Mr. McKee is an "audit committee financial expert" as defined by applicable SEC rules.

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. 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.

Stockholders may locate a current copy of our Code of Business Conduct and Ethics on our website at www.ceruleanrx.com or request a copy without charge from:

Cerulean Pharma Inc.
Attn: Vice President, General Counsel
840 Memorial Drive, 5th Floor
Cambridge, MA 02139

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our directors and certain officers and holders of more than 10% of our common stock to file with the SEC initial reports of ownership of our common stock and other equity securities on a Form 3 and reports of changes in such ownership on a Form 4 or Form 5. These Section 16 reporting persons are required by SEC regulations to furnish us with copies of all Section 16(a) forms they file. Based solely on a review of the copies of such forms received by us, and written representations from certain reporting persons, we believe that during 2014, our directors, officers and 10% stockholders complied with all Section 16(a) filing requirements applicable to them with respect to our common stock during that fiscal year.

Item 11. 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 and practices. 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 2014 are Oliver S. Fetzer, our former President and Chief Executive Officer, Christopher D.T. Guiffre, our Chief Operating Officer, Edward Garmey, our Senior Vice President and Chief Medical Officer and Karen L. Roberts, our Senior Vice President, Finance and Administration.

As a newly 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 are 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 years ended December 31, 2014 and 2013.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Option Awards ($)(2)	All Other Compensation ($)		Total ($)
Christopher D.T. Guiffre, J.D.	2014	317,128	115,500	387,336	11,168	(4)	831,132
Chief Operating Officer(3)	2013	295,000	73,750	—	10,968	(5)	379,718
Edward Garmey, M.D.	2014	309,000	98,880	243,390	11,168	(4)	662,438
Senior Vice President and	2013	303,000	75,750	—	10,968	(5)	389,718
Chief Medical Officer							
Karen L. Roberts	2014	242,000	59,895	260,782	11,168	(4)	573,845
Senior Vice President Finance	2013	230,000	57,500	—	10,968	(5)	298,468
and Administration							
Oliver S. Fetzer, Ph.D.	2014	324,438	—	1,614,215	14,785	(6)	1,953,438
Former President and	2013	352,000	176,000	146,088	10,968	(5)	685,056
Chief Executive Officer							

(1) The 2014 amount reflects the discretionary bonus earned in 2014 and paid in March 2015, and the 2013 amount reflects the discretionary bonus earned in 2013 and paid in March 2014. Due to his resignation effective October 29, 2014, Dr. Fetzer will not be paid bonus for 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 Annual Report on Form 10-K for assumptions underlying the valuation of equity awards.

(3) Mr. Guiffre served as our Senior Vice President and Chief Business Officer through October 28, 2014 and was named Chief Operating Officer on October 29, 2014.

(4) Consists of $10,400 that we matched pursuant to our 401(k) plan and $768 in life insurance premiums.

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

(6) Consists of 10,400 that we matched pursuant to our 401(k) plan, $640 in life insurance premiums and $3,745 accrued vacation paid at termination.

Narrative to summary compensation table

Base salary. In 2014, we paid base salaries of $317,128 to Mr. Guiffre, $309,000 to Dr. Garmey, $242,000 to Ms. Roberts, and $324,438 to Dr. Fetzer. 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 June 2014, our board of directors, upon the recommendation of our compensation committee, approved a 2014 base salary of $425,000 for Dr. Fetzer. In October 2014, our board of directors promoted Mr. Guiffre to Chief Operating Officer and approved a 2014 base salary of $350,000 for Mr. Guiffre.

In February 2015, our compensation committee approved 2015 base salaries of $364,000 for Mr. Guiffre, $321,360 for Dr. Garmey and $281,680 for Ms. Roberts.

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 2014, we awarded bonuses, payable in March 2015, of $115,500 to Mr. Guiffre, $98,880 to Dr. Garmey and $59,895 for Ms. Roberts, such amounts representing 83%, 80% and 83% of bonus targets for Mr. Guiffre, Dr. Garmey and Ms. Roberts, respectively. In each case, such bonuses are based on the combination of each of Mr. Guiffre's, Dr. Garmey's and Ms. Roberts' achievement of individual goals (25% of such bonus) and our attainment of corporate goals (75% of such bonus). Due to his resignation effective October 29, 2014, Dr. Fetzer was not awarded a bonus for fiscal year 2014.

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 our initial public offering, or IPO, which was completed in April 2014, our executive officers were eligible to participate in our 2007 stock incentive plan, as amended, or the 2007 Plan. Following the closing of our IPO, our employees and executives became eligible to receive stock options and other stock-based awards pursuant to the 2014 stock incentive plan, or our 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 our IPO, the award of stock options to our executive officers, other than our Chief Executive Officer, was made by our board or compensation committee, and the award of stock options to our Chief Executive Officer was made by our board. We have granted stock options to our executive officers with both time-based and performance-based vesting. Upon initiation of employment, the options that we have granted to our executive officers and other employees 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. Beginning in 2014, following our IPO, options that we grant to existing executive officers and other employees with time-based vesting typically vest ratably over 48 months from the vesting commencement date. None of our executive officers is currently party to an employment agreement that provides for automatic award of stock options. 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. 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. Following our IPO, the exercise prices of all stock options granted are equal to the fair market value of shares of our common stock on the date of grant, which is determined by reference to the closing market price of our common stock on the NASDAQ Global Market on the date of grant.

In February 2015, our compensation committee granted an option to purchase 75,000 shares of our common stock to Mr. Guiffre, an option to purchase 43,000 shares of our common stock to Dr. Garmey and an option to purchase 43,000 shares of our common stock to Ms. Roberts. These options have an exercise price of $8.16 per share and vest monthly as to 1/48th of the shares underlying the option over four years following the grant date.

2014 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, 2014:

	Option Awards				
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable		Option Exercise Price ($)	Option Expiration Date
Christopher D.T. Guiffre, J.D.	39,203	14,562	(1)	3.77	1/24/2022
	—	51,698	(2)	3.77	1/24/2022
	4,616	4,620	(3)	3.92	12/18/2022
	—	9,236	(4)	3.92	12/18/2022
	4,478	13,444	(3)	10.59	1/9/2024
	7,335	42,965	(5)	5.73	6/23/2024
	3,143	47,157	(6)	4.36	10/28/2024
Edward Garmey, M.D.	23,982	3,590	(7)	3.34	6/8/2021
	14,475	4,826	(8)	3.77	1/24/2022
	6,314	6,314	(3)	3.92	12/18/2022
	3,446	10,340	(9)	10.59	1/9/2024
	7,335	42,965	(5)	5.73	6/23/2024
Karen L. Roberts	9,650	—		3.34	3/3/2020
	10,560	—		3.34	1/27/2021
	10,339	3,447	(8)	3.77	1/24/2022
	7,346	7,347	(3)	3.92	12/18/2022
	3,446	10,340	(9)	10.59	1/9/2024
	5,570	32,630	(5)	5.73	6/23/2024
	2,931	17,169	(5)	4.98	7/16/2024
Oliver S. Fetzer, Ph.D.	95,981	—		5.95	9/30/2015
	25,546	—		3.34	9/30/2015
	93,949	8,265	(10)	3.34	9/30/2015
	31,750	14,433	(10)	3.77	9/30/2015
	14,669	2,098	(10)	3.92	9/30/2015
	—	126,309	(10)	3.92	9/30/2015
	24,166	265,834	(10)	5.73	9/30/2015
	5,169	13,280	(10)	10.59	9/30/2015
	—	9,123	(10)	10.59	9/30/2015

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

(2) 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.

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

(4) 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.

(5) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through May 31, 2018.

(6) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through September 30, 2018.

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

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

(9) The unvested shares underlying this option are scheduled to vest in approximately equal monthly installments through December 31, 2017.

(10) Pursuant to the terms of the separation agreement we entered into with Dr. Fetzer on October 29, 2014 and amended on March 3, 2015, the unvested shares underlying this option will not vest. Any unexercised vested shares and the unvested shares will expire on September 30, 2015.

Employment Agreements

Agreements with Mr. Guiffre, Dr. Garmey and Ms. Roberts

In July 2014, we entered into employment agreements with each of Mr. Guiffre, Dr. Garmey and Ms. Roberts in connection with their continuation of their employment with us. These agreements provide that each of Mr. Guiffre, Dr. Garmey and Ms. Roberts are employed at will, and either we or each of Mr. Guiffre, Dr. Garmey and Ms. Roberts may terminate the employment relationship for any reason, at any time, with or without notice.

Pursuant to such agreements, Mr. Guiffre, Dr. Garmey and Ms. Roberts are 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 Mr. Guiffre, Dr. Garmey and Ms. Roberts and which will be determined by our board of directors in its sole discretion. The target annual bonus for the applicable fiscal year is 45% of base salary for Mr. Guiffre, 40% of base salary for Dr. Garmey and 30% of base salary for Ms. Roberts.

If we terminate employment with Mr. Guiffre, Dr. Garmey or Ms. Roberts without cause or if Mr. Guiffre, Dr. Garmey or Ms. Roberts terminates employment with us for good reason, in each case, excluding following a change of control, upon execution and effectiveness of a release of claims, we are obligated to pay such individual (a) an amount equal to his or her base salary for six (6) months, payable in six (6) substantially equal monthly installments, and (b) the amount of any bonus for the prior year that was approved but not yet paid to such individual at the time of termination. We must also continue to provide such individual and certain of his or her dependents with group health insurance for a period of six (6) months following such termination.

If we terminate employment with Mr. Guiffre, Dr. Garmey or Ms. Roberts without cause or if Mr. Guiffre, Dr. Garmey or Ms. Roberts terminates employment with us for good reason, following a change of control, upon execution and effectiveness of a release of claims, we are obligated to pay such individual (a) an amount equal to his or her base salary for six (6) months, plus one (1) additional month for each year of service by such individual with us, up to a maximum of nine (9) months, payable in a lump sum payment, and (b) an amount equal to such individual's target performance-based annual bonus pro-rated to the severance period in months divided by twelve (12) months. We must also continue to provide such individual and certain of his or her dependents with group health insurance for the duration of the severance period and to accelerate in full the vesting of any outstanding equity awards that are subject to time-based vesting.

Separation, Transition and Release of Claims Agreement with Dr. Fetzer

Dr. Fetzer voluntarily resigned from his position as our President, Chief Executive Officer and director, effective October 29, 2014, or the separation date. In connection with Dr. Fetzer's termination of employment with us, we entered into a separation, transition, and release of claims agreement with him. To assist us in in our leadership transition, Dr. Fetzer agreed that for one hundred and eighty (180) days following the separation date, or the consulting period, he would make himself reasonably available to us by telephone or e-mail from time to time, upon reasonable notice and on an as-needed basis to provide us with any reasonable information and guidance that we may request from him. On March 3, 2015, we amended the separation, transition and release of claims agreement with Dr. Fetzer, to extend the consulting period until September 30, 2015. As a result of the extension of the consulting period until September 30, 2015, all stock options held by Dr. Fetzer, which ceased vesting as of the separation date, will remain exercisable until September 30, 2015.

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 provided 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 were eligible to receive awards under the 2007 Plan. However, incentive stock options could only be granted to our employees.

As of February 28, 2015, there were outstanding under the 2007 Plan options to purchase an aggregate of 1,038,486 shares of common stock at a weighted-average exercise price of $5.05 per share. We no longer grant stock options or other awards under the 2007 Plan. However, 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 become available for issuance under the 2014 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 and exercise price per share of each outstanding option 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.

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, 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 became effective upon our IPO. 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.

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

Our board of directors administers the 2014 Plan. Pursuant to the terms of the 2014 Plan, our board of directors selects the recipients of awards and determines:

- 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.

As of February 28, 2015, (i) there were 3,218,490 shares of our common stock reserved for issuance under the 2014 Plan and (ii) there were outstanding options to purchase an aggregate of 1,839,630 shares of common stock at a weighted-average exercise price of $6.09 per share.

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 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 became effective upon the IPO. Our board of directors administers the 2014 ESPP. 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.

As of February 28, 2015, there were 701,250 shares of our common stock reserved for issuance under the 2014 ESPP and no shares have been issued under this plan.

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 $17,500 for 2013 and 2014. Participants who are at least 50 years old can also make "catch-up" contributions, which in 2013 and 2014 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.

2014 Director Compensation

The following table sets forth information regarding compensation earned by our non-employee directors during 2014.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)	Total ($)
Alan L. Crane	37,500 (2)	— (3)	85,771
Paul A. Friedman, M.D.	51,693	300,450 (4)(5)	352,143
Steven E. Hall, Ph.D.	31,875	—	31,875
Susan L. Kelley, M.D.	9,273	33,850 (6)	43,123
William T. McKee	34,397	82,012 (5)	116,409
David Parkinson, M.D.	6,522	35,801 (7)	42,323
William H. Rastetter, Ph.D.	33,375	82,012 (5)	115,387
Ram Sasisekharan, Ph.D.	22,500	—	22,500
Robert I. Tepper, M.D.	30,000	—	30,000

(1) The amount reported in the "Option Awards" column reflects 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 Annual Report on Form 10-K for assumptions underlying the valuation of equity awards. Including these options, as of December 31, 2014:

- Mr. Crane held stock options to purchase 33,232 shares of common stock, which were vested with respect to 22,565 shares in the aggregate;
  Dr. Friedman held stock options to purchase 113,786 shares of common stock, all of which were unvested;
  Dr. Kelley held stock options to purchase 15,000 shares of common stock, all of which were unvested;
  Mr. McKee held stock options to purchase 13,786 shares of common stock, all of which were unvested;
  Dr. Parkinson held stock options to purchase 15,000 shares of common stock, all of which were unvested;
  Dr. Rastetter held stock options to purchase 13,786 shares of common stock, all of which were unvested; and
- Dr. Tepper held stock options to purchase 3,447 shares of common stock, all of which were fully vested.

(2) Mr. Crane served as Chairman of our Board until Dr. Friedman's appointment as Executive Chair in October 2014.

(3) In 2013, we granted an option to Mr. Crane in recognition of his services to us other than in his role as a director. In July 2014, this option was modified to reduce the number of shares to a total of 16,000 shares and to modify the vesting to time-based vesting beginning in March 2013 through March 2016. The amount of the incremental fair value of the amended option, computed in accordance with FASB ASC Topic 718, was $213.

(4) In October 2014, in connection with his appointment as Executive Chair of the board of the directors, we granted Dr. Friedman option to purchase 100,000 shares with an exercise price of $4.36 per share. The option will fully vest on the first anniversary of the grant date. Dr. Friedman also receives an annual cash retainer of $155,000 for his service as our Executive Chairman.

(5) 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.

(6) In October 2014, in connection with her election to our board, we granted Dr. Kelley an option to purchase 15,000 shares of our common stock with an exercise price of $4.74 per share. The option vests in three equal annual installments beginning on the first anniversary of Dr. Kelley's election.

(7) In October 2014, in connection with his election to our board, we granted Dr. Parkinson an option to purchase 15,000 shares of our common stock with an exercise price of $4.36 per share. The option vests in three equal annual installments beginning on the first anniversary of Dr. Parkinson's election.

Prior to his resignation in October 2014, Dr. Fetzer, one of our directors who also served as our President and Chief Executive Officer, did not receive any additional compensation for his service as a director.

Director compensation policy

Our board has established the following compensation policy for non-employee directors, which became effective upon the closing of our IPO:

- 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 clinical advisory committee will receive a cash retainer of $1,875 per year ($3,750 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 our IPO 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 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 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.

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.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The following table sets forth information with respect to the beneficial ownership of our common stock, as of February 28, 2015:

- 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.

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, 2015 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.

The percentage ownership calculations for beneficial ownership are based on 20,369,683 shares of common stock outstanding as of February 20, 2015.

Name and address of Beneficial Owner	Number of shares beneficially owned	Percentage of shares beneficially owned
5% Stockholders		
Entities affiliated with Polaris Partners (1)	4,724,968	23.2%
Entities affiliated with Venrock (2)	3,034,038	14.9%
FMR LLC (3)	2,431,400	11.9%
Entities affiliated with Lilly Ventures (4)	2,356,227	11.6%
Entities affiliated with Crown Ventures (5)	2,259,244	11.1%
Named Executive Officers and Directors		
Christopher D. T. Guiffre, J.D. (6)	75,929	*
Edward Garmey, M.D. (7)	74,005	*
Karen L. Roberts (8)	58,815	*
Paul A. Friedman, M.D. (9)	4,595	*
Alan L. Crane (10)	4,830,069	23.7%
Steven E. Hall, Ph.D. (11)	2,356,227	11.6%
Susan L. Kelley, M.D.	—	—
William T. McKee (12)	4,595	*
David R. Parkinson, M.D.	—	—
William H. Rastetter, Ph.D. (13)	65,281	*
Ram Sasisekharan, Ph.D.	82,715	*
Robert I. Tepper, M.D. (14)	22,401	*
All current executive officers and directors as a group (15)	7,574,632	37.2%

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

(1) Consists of (a) 1,405,750 shares of common stock held by Polaris Venture Partners IV, LP (“Polaris IV”), (b) 26,351 shares of common stock held by Polaris Ventures Partners Entrepreneurs’ Fund IV, LP (“Polaris EFund IV”), (c) 3,148,044 shares of common stock held by Polaris Venture Partners V, LP (“Polaris V”), (d) 61,353 shares of common stock held by Polaris Venture Partners Entrepreneurs’ Fund V, LP (“Polaris EFund V”), (e) 21,562 shares of common stock held by Polaris Ventures Partners Founders’ Fund V, LP (“Polaris FFund V”), (f) 31,478 shares of common stock held by 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”) and (g) 5,242, 98, 24,213, 471, 165 and 241 shares of common 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. 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) 2,720,455 shares of common stock held by Venrock Associates V, LP ("VA5"), (b) 230,647 shares of common stock held by Venrock Partners V, LP ("VP5"), (c) 63,915 shares of common stock held by Venrock Entrepreneurs V, LP ("VE5" and collectively with VA5 and VP5, the "Venrock Funds") and (d) 17,164, 1,454 and 403 shares of common stock issuable upon the exercise of warrants 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) Based on information supplied by FMR LLC on Schedule 13G filed with the SEC on May 12, 2014. Fidelity SelectCo, LLC ("SelectCo"), 1225 17th Street, Suite 1100, Denver, Colorado 80202, a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of 2,431,400 shares of our common stock as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940 (the "SelectCo Funds"). Edward C. Johnson 3d and FMR LLC, through its control of SelectCo, and the SelectCo Funds each has sole power to dispose of the 2,431,400 shares owned by the SelectCo Funds. The ownership of one investment company, Select Biotechnology Portfolio, amounted to 1,901,400 shares or 10.000% of the Common Stock outstanding. Select Biotechnology Portfolio has its principal business office at 245 Summer Street, Boston, Massachusetts 02210. Members of the family of Edward C. Johnson 3d, Chairman of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d, Chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Funds' Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Funds' Boards of Trustees

(4) Steven E. Hall is a general 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) 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, 2015.

(7) Consists of (a) 6,892 shares of common stock and (b) 67,113 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.

(8) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.

(9) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.

(10) Consists of (a) the shares described in note (1) above, (b) 77,201 shares of common stock and (c) 27,898 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.

(11) Consists of (a) the shares described in note (4) above. Dr. Hall is a general 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.

(12) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.

(13) Consists of (a) 60,307 shares of common stock (b) 379 shares of common stock issuable upon the exercise of warrants and (c) 4,595 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015. William H. Rastetter holds the aforementioned shares jointly as community property with his wife.

(14) Consists of (a) 18,954 shares of common stock and (b) 3,447 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.

(15) Consists of (a) 7,296,834 shares of common stock, (b) 30,811 shares of common stock issuable upon the exercise of warrants and (c) 246,987 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.

SECURITIES AUTHORIZED FOR ISSUANCE UNDER OUR EQUITY COMPENSATION PLANS

The following table provides information about the securities authorized for issuance under our equity compensation plans as of December 31, 2014.

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)		Weighted-average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)	
Equity compensation plans approved by security holders	2,126,176	(1)	$ 4.97	1,434,928	(2)
Equity compensation plans not approved by security holders	—		—	—	
Total	2,126,176		$ 4.97	1,434,928	

(1) Consists of stock options outstanding as of December 31, 2014 under our 2007 stock incentive plan and 2014 stock incentive plan.

(2) Consists of shares of common stock authorized under the 2014 stock incentive plan that remained available for grant under future awards as of December 31, 2014. This amount does not include an additional 831,932 shares that became available for issuance under the 2014 stock incentive plan on January 1, 2015 in accordance with the terms of the 2014 stock incentive plan. The number of shares available under the 2014 stock incentive plan is subject to further increase by (i) the number of shares of our common stock subject to outstanding awards under the 2007 stock incentive plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased and (ii) further annual increases, to be added on January 1 of each year, from and after 2016 through 2024, in each case 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.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Since January 1, 2014, 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.

Bridge Financings

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 Issued upon Conversion of 2014 Convertible Notes(1)
CVF, LLC	819,319	152,764
Entities affiliated with Polaris Partners(2)	2,151,000	401,061
Entities affiliated with Venrock(3).	1,381,200	257,529
Lilly Ventures Fund I LLC(4)	1,072,800	199,875
Entities affiliated with Lux Capital(5)	530,081	98,835
William H. Rastetter(6)	27,600	5,146

(1) The 2014 convertible notes converted into shares of our common stock at $5.43, which was equal to 77.5% of our initial public offering price of $7.00 per share.

(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 general 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 certain holders of our common stock (who were formerly holders of our preferred stock prior to our initial public offering and the conversion of such preferred stock into our common 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 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" in this Annual Report on Form 10-K for additional information regarding these rights.

Participation in Our Initial Public Offering

Certain of our director and principal stockholders and their affiliated entities purchased 4,113,172 shares of our common stock in our initial public offering at the initial public offering price of $7.00 per share. The following table sets forth the aggregate number of shares that our directors and 5% stockholders and their affiliated entities purchased.

Beneficial Owner	Number of Shares Purchased in Initial Public Offering
Entities affiliated with Polaris Partners (1)	1,470,582
Entities affiliated Venrock (2)	944,290
Entities affiliated with Lux Capital (3)	106,224
Entities affiliated with Lilly Ventures (4)	733,445
Entities affiliated with Crown Ventures	827,456
William H. Rastetter (5)	18,869

(1) Consists of (a) 1,419,015 shares of common stock held by Polaris Venture Partners V, L.P., (b) 27,657 shares of common stock held by Polaris Venture Partners Entrepreneurs' Fund V, L.P., (c) 9,720 shares of common stock held by Polaris Venture Partners Founders' Fund V, L.P. and (d) 14,190 shares of common stock held by Polaris Venture Partners Special Founders' Fund V, 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. and Polaris Venture Partners Special Founders' Fund V, L.P.

(2) Consists of (a) 852,033 shares of common stock held by Venrock Associates V, L.P., (b) 72,238 shares of common stock held by Venrock Partners V, L.P. and (c) 20,019 shares of common stock held by Venrock Entrepreneurs Fund V, L.P.

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

(4) Consists of (a) 89,577 shares of common stock held by Lux Ventures II, L.P., (b) 3,756 shares of common stock held by Lux Ventures II Sidecar, L.P. and (c) 12,891 shares of common stock held by Lux Ventures II Partners Fund I LLC.

(5) Consists of 18,869 shares of common stock held by William H. Rastetter and Marisa G. Rastetter as community property. Dr. Rastetter is a member of our board of directors.

Indemnification Agreements

Our certificate of incorporation 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

Our board of directors has adopted a written related person transaction policy that sets forth policies and procedures for the review and approval or ratification of related person transactions. This policy covers 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.

Prior to our initial public offering, we did not have a written policy regarding the review and approval of related person transactions. Nevertheless, with respect to such transactions, it was 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.

Director Independence

Rule 5605 of the NASDAQ Listing Rules requires a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the NASDAQ Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act and that compensation committee members also satisfy heightened independence requirements contained in the NASDAQ Listing Rules as well as Rule 10C-1 under the Exchange Act.

Under Rule 5605(a)(2), a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

When determining the independence of the members of our compensation committee under the heightened independence requirements contained in the NASDAQ Listing Rules and Rule 10C-1, our board of directors is required to consider all factors specifically relevant to determining whether a director has a relationship with us that is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of that director, including any consulting, advisory or other compensatory fee paid by us to that director; and (2) whether that director is affiliated with our company, a subsidiary of our company or an affiliate of a subsidiary of our company.

In March 2014, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. In October 2014, our board of directors further considered the independence of David Parkinson and Susan Kelley, respectively, in connection with their respective appointments to our board of directors. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Alan Crane, is an "independent director" as defined under Rule 5605(a)(2) of the NASDAQ Listing Rules.

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 of directors also determined that Steven E. Hall, William T. McKee and William H. Rastetter, who comprise our audit committee, Steven E. Hall and Robert I. Tepper, who comprise our compensation committee, and William T. McKee and William H. Rastetter, who compromise our nominating 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 our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.]

Item 14. Principal Accountant Fees and Services

The following table sets forth aggregate fees billed to us for services related to the fiscal years ended December 31, 2014 and 2013, by Deloitte & Touche LLP, our independent registered public accounting firm for periods.

	2014	2013
Audit Fees (1)	$ 360,152	$ 1,075,872
Audit Related Fees (2)	—	—
Tax Fees (3)	15,400	15,325
All Other Fees (4)	—	4,524
Total	$ 375,552	$ 1,095,721

(1) Audit Fees consist of fees billed for professional services performed by Deloitte & Touche LLP for the audit of our annual consolidated financial statements, the review of interim consolidated financial statements, and related services that are normally provided in connection with registration statements, including the registration statement for our initial public offering. Included in the 2013 Audit Fees is $478,772 of fees billed in connection with our initial public offering.

(2) Audit Related Fees may consist of fees billed by an independent registered public accounting firm for assurance and related services that are reasonably related to the performance of the audit or review of our consolidated financial statements. There were no such fees incurred by the company in 2014 or 2013.

(3) Tax Fees consist of fees for professional services, including tax consulting and compliance performed by an independent registered public accounting firm.

(4) All Other Fees for the year ended December 31, 2013 were for consulting services in connection with formation of our wholly owned subsidiary, Cerulean Pharma Australia Pty Ltd. There were no such fees incurred in 2014.

The audit committee has considered the services listed above to be compatible with maintaining Deloitte & Touche LLP's independence.

Pre-Approval Policy and Procedures

Our audit committee has established a policy that all audit and permissible non-audit services provided by our independent registered public accounting firm will be pre-approved by the audit committee, and all such services were pre-approved in accordance with this policy during the fiscal year ended December 31, 2014. These services may include audit services, audit-related services, tax services and other services. The audit committee considers whether the provision of each non-audit service is compatible with maintaining the independence of our auditors. Pre-approval is detailed as to the particular service or category of services and is generally subject to a specific budget. Our independent registered public accounting firm and management are required to periodically report to the audit committee regarding the extent of services provided by the independent registered public accounting firm in accordance with this pre-approval, and the fees for the services performed to date.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a)(1) Financial Statements

Our consolidated financial statements are set forth in Part II, Item 8 of this Annual Report on Form 10-K and are incorporated herein by reference.

(a)(2) Financial Statement Schedules

All financial schedules have been omitted because the required information is either presented in the consolidated financial statements or the notes thereto or is not applicable or required.

(a)(3) Exhibits

The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the exhibits and are incorporated herein.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

CERULEAN PHARMA INC.

By: /s/ Christopher D. T. Guiffre

Christopher D. T. Guiffre, J.D.
Chief Operating Officer
(Principal Executive Officer)

Date: March 19, 2015

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

/s/ Christopher D. T. Guiffre *Christopher D. T. Guiffre, J.D.*	Chief Operating Officer *(Principal Executive Officer)*	March 19, 2015
/s/ Karen L. Roberts *Karen L. Roberts*	Senior Vice President, Finance and Administration *(Principal Financial and Accounting Officer)*	March 19, 2015
/s/ Paul A. Friedman *Paul A. Friedman, M.D.*	Director	March 19, 2015
/s/ William H. Rastetter *William H. Rastetter, Ph.D.*	Director	March 19, 2015
/s/ Alan L. Crane *Alan L. Crane*	Director	March 19, 2015
/s/ Steven E. Hall *Steven E. Hall, Ph.D.*	Director	March 19, 2015
/s/ Susan L. Kelley *Susan L. Kelley, M.D.*	Director	March 19, 2015
/s/ William T. McKee *William T. McKee*	Director	March 19, 2015
/s/ David Parkinson *David Parkinson, M.D.*	Director	March 19, 2015
/s/ Ram Sasisekharan *Ram Sasisekharan, Ph.D.*	Director	March 19, 2015
/s/ Robert I. Tepper *Robert I. Tepper, M.D.*	Director	March 19, 2015

Exhibit Index

Exhibit Number	Description of Exhibit	Incorporated By Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation	8-K	001-36395	April 16, 2014	3.1	
3.2	Amended and Restated By-Laws	8-K	001-36395	April 16, 2014	3.2	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-194442	March 31, 2014	4.1	
10.1#	2007 Stock Incentive Plan, as amended	S-1	333-194442	March 10, 2014	10.1	
10.2#	Form of Incentive Stock Option Agreement under 2007 Stock Incentive Plan	S-1	333-194442	March 10, 2014	10.2	
10.3#	Form of Nonstatutory Stock Option Agreement under 2007 Stock Incentive Plan	S-1	333-194442	March 10, 2014	10.3	
10.4#	2014 Stock Incentive Plan	S-1	333-194442	March 31, 2014	10.4	
10.5#	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan	S-1	333-194442	March 31, 2014	10.5	
10.6#	Form of Nonstatutory Stock Option Agreement under 2014 Stock Incentive Plan	S-1	333-194442	March 31, 2014	10.6	
10.7#	2014 Employee Stock Purchase Plan	S-1	333-194442	March 31, 2014	10.26	
10.8†	License Agreement, dated as of May 22, 2000, as amended, between California Institute of Technology and Insert Therapeutics, Inc.	S-1	333-194442	March 10, 2014	10.7	
10.9†	Exclusive Patent License Agreement, dated as of December 21, 2006, as amended, between the Registrant and Massachusetts Institute of Technology	S-1	333-194442	March 10, 2014	10.8	
10.10†	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	S-1	333-194442	March 10, 2014	10.9	
10.11†	IT-101 Agreement, dated as of June 23, 2009, as amended, between the Registrant and Calando Pharmaceuticals, Inc.	S-1	333-194442	March 10, 2014	10.10	
10.12†	Platform Agreement, dated as of June 23, 2009, as amended, between the Registrant and Calando Pharmaceuticals, Inc.	S-1	333-194442	March 10, 2014	10.11	
10.13†	Letter Agreement, dated as of August 6, 2013, between the Registrant and California Institute of Technology	S-1	333-194442	March 10, 2014	10.12	
10.14	Second Series D Convertible Preferred Stock Purchase Agreement, dated November 30, 2012, as amended	S-1	333-194442	March 10, 2014	10.13	
10.15	Commercial Lease Agreement, dated September 8, 2009, between the Registrant and Rivertech Associates II, LLC	S-1	333-194442	March 10, 2014	10.14	

10.16	Second Lease Amendment to the Commercial Lease Agreement between the Registrant and Rivertech Associate II, LLC, dated July 11, 2014.	8-K	001-36395	July 17, 2014	10.1	
10.17	Loan and Security Agreement, dated January 8, 2015, between the Registrant and Hercules Technology Growth Capital, Inc.	8-K	001-36395	January 8, 2015	10.1	
10.18	Stock Purchase Agreement, dated January 8, 2015, between the Registrant and Hercules Technology Growth Capital, Inc.	8-K	001-36395	January 8, 2015	10.2	
10.19	Right to Invest Letter, dated January 8, 2015, between the Registrant and Hercules Technology Growth Capital, Inc.	8-K	001-36395	January 8, 2015	10.3	
10.20#	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors	S-1	333-194442	March 10, 2014	10.16	
10.21#	Separation, Transition and Release of Claims Agreement, dated October 29, 2014, by and between the Company and Oliver S. Fetzer, Ph.D.	8-K	001-36395	October 30, 2014	10.1	
10.22	Warrant to purchase shares of Series B Convertible Preferred Stock issued by the Registrant to Silicon Valley Bank	S-1	333-194442	March 10, 2014	10.18	
10.23	Form of Stock Purchase Warrant of the Registrant to purchase shares of Series C Convertible Preferred Stock	S-1	333-194442	March 10, 2014	10.19	
10.24	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	S-1	333-194442	March 10, 2014	10.20	
10.25	Warrant, dated January 8, 2015, issued to Hercules Technology Growth Capital, Inc.	8-K	001-36395	January 8, 2015	4.1	
10.26#	Employment Agreement dated July 21, 2014 by and between the Registrant and Christopher D. T. Guiffre	10-Q	001-36395	November 13, 2014	10.2	
10.27#	Employment Agreement dated July 21, 2014 by and between the Registrant and Edward Garmey	10-Q	001-36395	November 13, 2014	10.3	
10.28#	Employment Agreement dated July 21, 2014 by and between the Registrant and Karen Roberts					X
10.29#	Stock Option Agreement and Contingent Consideration Award Agreement, dated March 31, 2013, between the Registrant and Alan Crane	S-1	333-194442	March 10, 2014	10.24	
10.30#	Amendment to the Stock Option Agreement and Termination of Contingent Consideration Award dated September 16, 2014, by and between the Registrant and Alan Crane	10-Q	001-36395	November 13, 2014	10.4	

10.31	Fifth Amendment, dated as of February 17, 2015, to Exclusive Patent License Agreement, dated as of December 21, 2006, as amended, between the Registrant and Massachusetts Institute of Technology					X
10.32	Loan and Security Agreement, entered into as of December 6, 2011, as amended, between the Registrant and Lighthouse Capital Partners VI, L.P.	S-1	333-194442	March 10, 2014	10.15	
21.1	Subsidiaries of the Registrant					X
23.1	Consent of Deloitte & Touche LLP					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d 14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS*	XBRL Instance Document	10-K	001-36395	March 19, 2015	101.INS	X
101.SCH*	XBRL Taxonomy Extension Schema Document	10-K	001-36395	March 19, 2015	101.SCH	X
101.CAL*	XBRL Taxonomy Calculation Linkbase Document	10-K	001-36395	March 19, 2015	101.CAL	X
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document	10-K	001-36395	March 19, 2015	101.DEF	X
101.LAB*	XBRL Taxonomy Label Linkbase Document	10-K	001-36395	March 19, 2015	101.LAB	X
101.PRE*	XBRL Taxonomy Presentation Linkbase Document	10-K	001-36395	March 19, 2015	101.PRE	X

† Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

Management contracts or compensatory plans or arrangements required to be filed as an exhibit hereto pursuant to Item 15(a) of Form 10-K.

Exhibit 10.28

EMPLOYMENT AGREEMENT

THIS EMPLOYMENT AGREEMENT (the "Agreement"), made this 21st day of July, 2014, is entered into by Cerulean Pharma Inc., a Delaware corporation with its principal place of business at 840 Memorial Drive, 5th Floor, Cambridge, MA 02139 (the "Company"), and Karen Roberts (the "Employee").

The Company desires to continue to employ the Employee and the Employee desires to continue to be employed by the Company. In consideration of the mutual covenants and promises contained herein, and other good and valuable consideration, the receipt and sufficiency of which are acknowledged by the parties hereto, the parties agree as follows:

1. Term of Employment. The Company hereby agrees to continue to employ the Employee and the Employee hereby accepts continued employment with the Company, upon the terms set forth in this Agreement. There shall be no definite term of employment, and the Employee's employment shall be at-will such that both the Company and the Employee remain free to end the employment relationship for any reason, at any time, with or without notice.

2. Title and Capacity. The Employee shall serve as Senior Vice President, Finance and Administration of the Company and shall report to the Chief Executive Officer of the Company. The Employee shall be based at the Company's headquarters in Cambridge, Massachusetts.

The Employee agrees to undertake the duties and responsibilities inherent in such position and such other duties and responsibilities as the Chief Executive Officer or the Board of Directors of the Company (the "Board") shall from time to time reasonably assign to her. The Employee agrees to devote her entire business time, attention and energies to the business and interests of the Company. The Employee agrees to abide by the rules, regulations, instructions, personnel practices and policies of the Company and any changes therein that may be adopted from time to time by the Company.

3. Compensation and Benefits.

3.1 Base Salary. The Company shall pay the Employee, in accordance with the Company's regular payroll practices, a base salary at the annualized rate of $242,000, subject to adjustment thereafter by the Board.

3.2 Bonus. In addition to a base salary, the Employee will be eligible to receive a performance-based annual bonus for each fiscal year in which she is employed by the Company in the capacity of Senior Vice President, Finance and Administration. This bonus shall be based upon reasonably attainable annual quantitative and qualitative performance objectives established by the Board. The Employee's annual bonus level target shall be set at thirty percent (30%) of the Employee's base salary for the currently applicable fiscal year and shall be subject to adjustment thereafter by the Board. The Board will determine, in its sole discretion, based upon its review of the achievement of the performance objectives for a given fiscal year and its consideration of the recommendation of the Compensation Committee, whether (and in what amount) a bonus award is payable to the Employee.

To be eligible to receive a bonus award, the Employee must be an active employee on the date any such bonuses are distributed.

3.3 Employee Benefits. The Employee shall be entitled to participate in all benefit plans and programs that the Company establishes and makes available to its employees to the extent that the Employee is eligible under (and subject to the provisions of) the plan documents governing those programs. The Employee shall be entitled to twenty (20) days paid vacation per year plus personal days and paid holidays generally offered by the Company to its employees, each to be administered in accordance with Company policy.

3.4 Reimbursement of Expenses. The Company shall reimburse the Employee for all reasonable travel, entertainment and other expenses incurred or paid by the Employee in connection with, or related to, the performance of her duties, responsibilities or services under this Agreement in accordance with the Company's expense reimbursement policies as set forth in the Company's employee handbook, a copy of which has been provided to the Employee. The reimbursement of expenses hereunder shall be subject to the terms and conditions set forth in Section 18(e) of this Agreement.

3.5 Withholding. All salary, bonus and other compensation or benefits payable to the Employee shall be subject to applicable withholdings and taxes.

4. Payments Upon Resignation By The Employee Without Good Reason or Termination By The Company For Cause.

4.1 Payment upon Voluntary Resignation or Termination for Cause. If the Employee voluntarily resigns her employment other than for Good Reason (as defined in Section 4.2), or if the Company terminates the Employee for Cause (as defined in Section 4.3), the Company shall pay the Employee all accrued and unpaid base salary through the Employee's date of termination and any vacation that is accrued but unused as of such date. The Employee shall not be eligible for any severance or separation payments (including, but not limited to, those described in Sections 5 and 7 of this Agreement) or any continuation of benefits (other than those provided for under the Federal Consolidated Omnibus Budget Reconciliation Act ("COBRA")), or any other compensation pursuant to this Agreement or otherwise. The Employee also shall have such rights, if any, with respect to outstanding equity awards as may be provided under the agreement applicable to each.

4.2 Definition of "Good Reason". For purposes of this Agreement, "Good Reason" means the occurrence, without the Employee's written consent, of any of the events or circumstances set forth in clauses (a) through (c) below, provided, however, that an event described in clauses (a) through (c) below shall not constitute Good Reason unless it is communicated in writing, within 90 days of the first occurrence of an event giving rise to the claim, by the Employee to the Board or its successor and unless it is not corrected by the Company or its successor within thirty (30) days of the Company's receipt of such written notice:

(a) the material diminution of the Employee's duties, authority or responsibilities;

(b) a material reduction in the Employee's base salary; or

(c) a change by the Company in the location at which the Employee performs her principal duties for the Company to a new location that is both (i) outside a radius of 50 miles from the Employee's principal residence and (ii) more than 30 miles from the location at which the Employee performed her principal duties for the Company.

If the Company fails to timely correct an event of Good Reason, the termination of Executive's employment shall become effective 60 days after such notice is received by the Company.

4.3 Definition of "Cause". For purposes of this Agreement, "Cause" is defined as: (i) a good faith finding by the Board (excluding the Employee, if applicable) of (a) the Employee's failure to (1) perform reasonably assigned lawful duties or (2) comply with a lawful instruction of the Board so long as, in the case of (2), the instruction is consistent with the scope and responsibilities of the Employee's position, or (b) the Employee's dishonesty, willful misconduct or gross negligence, or (c) the Employee's substantial and material failure or refusal to perform according to, or to comply with, the policies, procedures or practices established by the Company or the Board and, in the case of (a) or (c), the Employee has had ten (10) days written notice to cure her failure to so perform or comply; or (ii) the Employee's indictment, or the entering of a guilty plea or plea of "no contest" with respect to a felony or any crime involving moral turpitude.

5. Termination Without Cause; Resignation for Good Reason. If the Employee's employment with the Company is terminated by the Company without Cause (as defined in Section 4.3), or by the Employee's voluntary resignation for Good Reason (as defined in Section 4.2), other than in connection with a Change in Control (as defined in Section 7.2(a)), then the Employee shall be paid all accrued and unpaid base salary and any accrued but unused vacation through the date of termination. In addition, subject to the Employee's execution and non-revocation of a binding severance and mutual release agreement in a form satisfactory to the Company (hereinafter, a "Severance Agreement") and subject to the terms and conditions of Section 18 of this Agreement, the Employee shall be eligible to receive the following separation benefits:

5.1 (a) an amount equal to the product of (i) one twelfth (1/12) of the Employee's then-current annualized base salary (provided, however, that if Employee's employment is terminated by the Employee's voluntary resignation for Good Reason as a result of the Company's material reduction of the Employee's base salary, then the Employee's then-current annualized base salary shall refer to her base salary as in effect immediately before such material reduction took effect) and (ii) six (6), less any amounts required to be withheld under applicable law, which amount shall be payable in six (6) substantially equal monthly installments, in accordance with the Company's payroll practices in effect from time to time beginning on the Payment Commencement Date (as defined below); and (b) the amount of any bonus for the prior year that was approved but not yet paid to the Employee at the time of the Employee's termination of employment, less any amounts required to be withheld under applicable law, which amount shall be paid in a manner and timing consistent with the payments to other similarly situated employees and consistent with the requirements of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code") but in no event later than March 15 of the year following the year of performance; provided, in both cases, that the Severance Agreement has been executed and any applicable revocation period with respect thereto has expired within sixty (60) days following the Employee's date of termination (such 60th day, the "Payment Commencement Date"); provided, however, that if the 60th day following the Employee's date of termination occurs in the calendar year following the year of termination, then the Payment Commencement Date shall be no earlier than January 1 of the year following the year of termination; and

5.2 upon the Employee's termination from employment pursuant to this Section 5, the Company shall make contributions to the cost of COBRA (Consolidated Omnibus Budget Reconciliation Act) coverage on behalf of the Employee and any applicable

dependents for a period of six (6) months after the Employee's termination if the Employee elects COBRA coverage, and only for so long as such coverage continues in force; provided, however, that if the Employee commences new employment and is eligible for a new group health plan, the Company's contributions toward COBRA coverage shall end when the new employment begins. The cost of COBRA shall be determined on the same basis as the Company's contribution to Company-provided health and dental insurance coverage in effect immediately before termination of the Employee's employment for an active employee with the same coverage elections. At the end of the six (6) month period, the Employee may continue such COBRA, if applicable, and shall be responsible for all premiums thereafter.

6. Termination by Reason of Death or Disability.

6.1 If the Employee's employment with the Company is terminated by reason of the Employee's death or Disability (as defined below), then the Employee (or her estate, if applicable) shall be paid, within thirty (30) days of the date of the Employee's death or determination of Disability, all accrued and unpaid base salary and any accrued but unused vacation through the date of termination.

6.2 For purposes of this Agreement, "Disability" shall mean the Employee's absence from the full-time performance of the Employee's duties with the Company for 180 consecutive calendar days as a result of incapacity due to mental or physical illness which is determined to be total and permanent by a physician selected by the Company or its insurers and acceptable to the Employee or the Employee's legal representative.

7. Termination Following Change of Control.

7.1 Benefits to Employee Upon a Change of Control Termination. In the event of a Change of Control Termination (as defined in Section 7.2(c) below), the Employee shall be entitled to all accrued and unpaid base salary and any accrued but unused vacation through the date of termination. In addition, subject to the Employee's execution and non-revocation of a binding Severance Agreement and subject to the terms and conditions of Section 18 of this Agreement, the Employee shall be eligible to receive the following separation benefits:

(a) an amount equal to the product of (i) one twelfth (1/12) of the Employee's then-current annualized base salary (provided, however, that if Employee's employment is terminated by the Employee's voluntary resignation for Good Reason as a result of the Company's material reduction of the Employee's base salary, then the Employee's then-current annualized base salary shall refer to her base salary as in effect immediately before such material reduction took effect) and (ii) the Severance Period (as defined in Section 7.2(d) below), less any amounts required to be withheld under applicable law, which amount shall be payable, in full and in a lump-sum cash payment on the Payment Commencement Date; provided, however, that if the Employee's date of termination occurs prior to the closing of the Change of Control, then the severance payable hereunder shall be paid in the manner set forth in Section 5.1(a); and

(b) an amount equal to the product of (i) the Employee's target performance-based annual bonus pursuant to Section 3.2 for the year in which the Employee's date of termination occurs and (ii) a fraction, the numerator of which is the number equal to the Severance Period and the denominator of which is twelve (12), less any amounts required to be withheld under applicable law, which amount shall be payable, in full and in a lump-sum cash payment on the Payment Commencement Date;

(c) contributions to the cost of COBRA coverage as provided in section 5.2 hereof, provided that in the event of a Change of Control Termination, such contributions shall last for the duration of the Severance Period; and

(d) full and immediate vesting of any equity awards subject to time-based vesting that are outstanding at the time of the termination of the Employee's employment. Any of the Employee's outstanding awards at the time of the termination will remain exercisable following termination to the extent set forth in the applicable award agreements.

7.2 Key Definitions. As used herein, the following terms shall have the following respective meanings:

(a) "Change in Control" means an event or occurrence set forth in any one or more of subsections (i) through (iii) below (including an event or occurrence that constitutes a Change in Control under one of such subsections but is specifically exempted from another such subsection), provided that such event constitutes a "change in control event" within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i):

(i) the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended (the "Exchange Act")) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 promulgated under the Exchange Act) more than 50% of either (x) the then-outstanding shares of common stock of the Company (the "Outstanding Company

Common Stock") or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); or

(ii) the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company in one or a series of transactions (a "Business Combination"), unless, immediately following such Business Combination, all or substantially all of the individuals and entities who were the beneficial owners of the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination beneficially own, directly or indirectly, more than 50% of the then-outstanding shares of common stock and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in such Business Combination (which shall include, without limitation, a corporation which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) (such resulting or acquiring corporation is referred to herein as the "Acquiring Corporation") in substantially the same proportions as their ownership, immediately prior to such Business Combination, of the Outstanding Company Common Stock and Outstanding Company Voting Securities, respectively; or

(iii) approval by the stockholders of the Company of a complete or substantially complete liquidation or dissolution of the Company.

(b) "Change in Control Date" means the first date during the period of time the Employee is employed pursuant to this Agreement on which a Change in Control occurs. Anything in this Agreement to the contrary notwithstanding, if (a) a Change in Control occurs, (b) the Employee's employment with the Company is terminated prior to the date on which the Change in Control occurs, and (c) it is reasonably demonstrated by the Employee that such termination of employment (i) was at the request of a third party who has taken steps reasonably calculated to effect a Change in Control or (ii) otherwise arose in connection with or in anticipation of a Change in Control, then for all purposes of this Agreement the "Change in Control Date" shall mean the date immediately prior to the date of such termination of employment.

(c) Change of Control Termination occurs where the Employee is terminated without Cause (as defined in Section 4.3) or resigns for Good Reason (as defined in Section 4.2), in either case within twelve (12) months following the Change in Control Date.

(d) "Severance Period" means six (6) months plus one (1) additional month for each year of service by the Employee with the Company, up to a maximum of nine (9) months.

8. Mitigation. The Employee shall not be required to mitigate the amount of any payment or benefits provided for in Sections 5 or 7 by seeking other employment or otherwise except with regard to medical and dental coverage if new employment is obtained.

9. Survival. The provisions of Sections 5 and 7 shall survive the termination of this Agreement for any reason.

10. Invention and Non-Disclosure Agreement. The Employee and the Company acknowledge (a) that they have entered into an Invention and Non-Disclosure Agreement and (b) the continuing effectiveness of such Invention and Non-Disclosure Agreement.

11. Notices. Any notices delivered under this Agreement shall be deemed duly delivered three (3) business days after it is sent by registered or certified mail, return receipt requested, postage prepaid, or one (1) business day after it is sent for next-business day delivery signature required via a reputable nationwide overnight courier service, to the Company's address set forth in the introductory paragraph hereto or to the home address of the Employee then on file with the Company, as applicable. Either party may change the address to which notices are to be delivered by giving notice of such change to the other party in the manner set forth in this Section 11.

12. Pronouns. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular forms of nouns and pronouns shall include the plural, and vice versa.

13. Entire Agreement. This Agreement and all exhibits hereto constitute the entire agreement between the parties and supersedes all prior agreements and understandings, whether written or oral, relating to the subject matter of this Agreement.

14. Amendment. This Agreement may be amended or modified only by a written instrument executed by both the Company and the Employee.

15. Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to the conflict of laws provisions thereof). Any action, suit or other legal proceeding arising under or relating to any provision of this Agreement shall be commenced only in a court of the Commonwealth of Massachusetts (or, if

appropriate, a federal court located within the Commonwealth of Massachusetts), and the Company and the Employee each consents to the jurisdiction of such a court. The Company and the Employee each hereby irrevocably waive any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this Agreement.

16. Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of both parties and their respective successors and assigns, including any corporation with which or into which the Company may be merged or which may succeed to its assets or business; provided, however, that the obligations of the Employee are personal and shall not be assigned by her.

17. Acknowledgment. The Employee states and represents that she has had an opportunity to fully discuss and review the terms of this Agreement with an attorney. The Employee further states and represents that she has carefully read this Agreement, understands the contents herein, freely and voluntarily assents to all of the terms and conditions hereof, and signs her name of her own free act.

18. Payments Subject to Section 409A. Subject to the provisions in this Section 18, any severance payments or benefits under this Agreement shall begin only upon the date of the Employee's "separation from service" (determined as set forth below) which occurs on or after the date of termination of the Employee's employment. The following rules shall apply with respect to distribution of the payments and benefits, if any, to be provided to the Employee under this Agreement:

(a) It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A of the Code and the guidance issued thereunder ("Section 409A"). Neither the Company nor the Employee shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(b) If, as of the date of the Employee's "separation from service" from the Company, the Employee is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement.

(c) If, as of the date of the Employee's "separation from service" from the Company, the Employee is a "specified employee" (within the meaning of Section 409A), then:

(i) Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation § 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid in the manner (and at the times) set forth in this agreement; and

(ii) Each installment of the severance payments and benefits due under this Agreement that is not described in paragraph c(i) above and that would, absent this subsection, be paid within the six-month period following the Employee's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, the Employee's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following the Employee's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation § 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation § 1.409A-1(b)(9)(iii) must be paid no later than the last day of the Employee's second taxable year following the taxable year in which the separation from service occurs.

(d) The determination of whether and when the Employee's separation from service from the Company has occurred shall be made and in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation § 1.409A-1(h).

(e) All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirements that (i) any reimbursement is for expenses incurred during the Employee's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

(f) Notwithstanding anything herein to the contrary, the Company shall have no liability to the Employee or to any other person if the payments and benefits provided hereunder that are intended to be exempt from or compliant with Section 409A are not so exempt or compliant.

19. Miscellaneous.

19.1 No delay or omission by the Company in exercising any right under this Agreement shall operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion shall be effective only in that instance and shall not be construed as a bar to or waiver of any right on any other occasion.

19.2 The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

19.3 In case any provision of this Agreement shall be invalid, illegal or otherwise unenforceable, the validity, legality and enforceability of the remaining provisions shall in no way be affected or impaired thereby.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the day and year set forth above.

CERULEAN PHARMA INC.

By: */s/ Oliver Fetzer*
Title: President & CEO

EMPLOYEE

/s/ Karen Roberts
Karen Roberts

FIFTH AMENDMENT

This Fifth Amendment, with the effective date of February 17, 2015, is to the Exclusive License Agreement dated December 21, 2006, as amended by a First Amendment dated July 30, 2007, a Second Amendment dated June 1, 2008, a Third Amendment dated June 30, 2009, and a Fourth Amendment dated August 1, 2013 (the "License Agreement") between Massachusetts Institute of Technology ("MIT") and Cerulean Pharma Inc. (formerly known as Tempo Pharmaceuticals Inc., "COMPANY"). Capitalized terms used herein and not otherwise defined shall have the meanings given such terms in the License Agreement.

Whereas, COMPANY has represented to MIT that it continues to devote substantial resources in an attempt to develop nanotechnology therapeutic products based on the technology of the Patent Rights.

Therefore, COMPANY and MIT agree to amend certain provisions of the Third Amendment to the License Agreement to extend certain deadlines as follows:

1. Section 2 of the Third Amendment shall be replaced in its entirety as follows:

The diligence terms of Sections 3(b), 3(c), 3(f), 3(g), 3(h), 3(i) and 3(j) shall be deleted in their entirety, but with the understanding that new diligence terms shall be agreed upon by the parties in accordance with Section 2 below by September 30, 2015.

2. Section 4 of the Third Amendment shall be replaced in its entirety as follows:

By June 1, 2015, COMPANY shall present to MIT a plan for development of Licensed Products under the PATENT RIGHTS which is satisfactory to MIT and a proposal for new diligence terms for development of Licensed Products. Thereupon, COMPANY and MIT shall negotiate in good faith the new diligence terms, which terms, once agreed upon, shall be added by further amendment to the License Agreement. In the event that COMPANY and MIT are unable to agree on new diligence terms by September 30, 2015, MIT may, at its sole discretion, terminate the License Agreement immediately upon written notice to COMPANY.

3. Section 6 of the Third Amendment shall be replaced in its entirety as follows

If at any time prior to September 30, 2015, if MIT becomes aware of a third party wishing to have a license to the Patent Rights to develop Licensed Products; and provided that (a) COMPANY has not provided MIT with a satisfactory plan for development of the Patent Rights according to Section 4 above; and (b) COMPANY is not in active negotiations with the third party at the time that MIT becomes aware of the third party's wishes for a license; then:

(i) MIT shall request from both COMPANY and the third party, development plans to bring one or more Licensed Products to market;

(ii) MIT shall evaluate the development plans based on capability and commitment of each party to develop Licensed Products and bring them to market, and shall choose the plan it considers to be in the best interests of the commercialization of the Patent Rights, at its sole discretion; and

(iii) if the third party's plan is considered superior to that of COMPANY, MIT may, at its sole discretion, either terminate the License Agreement or limit the Field of Use or exclusivity of the License Agreement.

4. Except as specifically modified or amended hereby, all other terms and conditions of the License Agreement shall remain unchanged and in full force and effect.

IN WITNESS WHEREOF, the parties have caused this Fifth Amendment to be executed under seal by their duly authorized representatives.

MASSACHUSETTS INSTITUTE OF TECHNOLOGY		CERULEAN PHARMA INC.	
By:	/s/ Lita Nelson	By:	/s/ Alejandra Carvajal
Name:	Lita Nelson	Name:	Alejandra Carvajal
Title:	Director, Technology Licensing Office	Title:	General Counsel
Date:	Feb 20, 2015	Date:	2/23/15

Exhibit 21.1

Subsidiaries of Cerulean Pharma Inc.

Name	Jurisdiction of Organization
Cerulean Pharma Australia Pty Ltd	Australia

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-198126 on Form S-8 of our report dated March 19, 2015, relating to the consolidated financial statements of Cerulean Pharma Inc. appearing in this Annual Report on Form 10-K of Cerulean Pharma Inc. for the year ended December 31, 2014.

/s/ DELOITTE & TOUCHE LLP

Boston, Massachusetts
March 19, 2015

Exhibit 31.1

CERTIFICATION

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

1. I have reviewed this Annual Report on Form 10-K of Cerulean Pharma Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 19, 2015

/s/ Christopher D. T. Guiffre

Christopher D.T. Guiffre
Chief Operating Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION

I, Karen L. Roberts, certify that:

1. I have reviewed this Annual Report on Form 10-K of Cerulean Pharma Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 19, 2015

/s/ Karen L. Roberts

Karen L. Roberts
Senior Vice President, Finance and Administration
(principal financial officer)

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Cerulean Pharma Inc. (the "Company") for the year ended December 31, 2014, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Christopher D.T. Guiffre, Chief Operating Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his knowledge on the date hereof:

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

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

Date: March 19, 2015

/s/ Christopher D. T. Guiffre
Christopher D.T. Guiffre
Chief Operating Officer
(principal executive officer)

Exhibit 32.2

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

In connection with the Annual Report on Form 10-K of Cerulean Pharma Inc. (the "Company") for the year ended December 31, 2014, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Karen L. Roberts, Senior Vice President, Finance and Administration of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to her knowledge on the date hereof:

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

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

Date: March 19, 2015

/s/ Karen L. Roberts
Karen L. Roberts
Senior Vice President, Finance and Administration
(principal financial officer)