CERULEAN PHARMA INC.

FORM 10-K
(Annual Report)

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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, 2016

Or

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

For the transition period from to

Commission File 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.)**
35 Gatehouse Drive Waltham, MA	**02451**
(Address of principal executive offices)	**(Zip Code)**

781-996-4300

(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, 2016 was approximately $47,569,338, based on the closing price of the registrant's common stock on The NASDAQ Global Market.

As of March 24, 2017, there were 29,021,455 of the Registrant's common shares, $0.0001 par value, issued and outstanding.

Documents incorporated by reference:

Portions of the registrant's definitive proxy statement, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission no later than April 30, 2017 in connection with its 2017 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

P ART 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 potential closing of strategic transactions with Daré Bioscience, Inc. and Novartis Institutes for BioMedical Research, Inc., the clinical development of any product candidates we may choose to develop, statements about our estimated research and development expenses and sufficiency of cash to fund operations, debt service, other scheduled expenditures 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: whether we are able to satisfy the closing conditions for the applicable strategic transaction, including obtaining the approval of our stockholders; whether our cash resources will be sufficient to fund our continuing operations for the period anticipated; 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

We are an oncology-focused company applying our proprietary Dynamic Tumor Targeting™ Platform, or the 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.

Recent Developments

In February 2017, we announced that our board of directors initiated a review of strategic alternatives that could result in changes to our business strategy and future operations. As part of this process, our board determined to review alternatives with the goal of maximizing stockholder value, including a potential sale of the company, a reverse merger, a business combination or a sale, license or other disposition of company assets.

On March 19, 2017, we entered into a stock purchase agreement, or the Stock Purchase Agreement, with Daré Bioscience, Inc., or Daré, and the holders of capital stock and securities convertible into capital stock of Daré named therein, or the Selling Stockholders, pursuant to which, among other things, the Selling Stockholders agreed to sell to us, and we agreed to purchase from the Selling Stockholders, all of the outstanding shares of capital stock, including those issuable upon conversion of convertible securities, of Daré. We refer to this transaction as the Daré Transaction. Subject to the terms and conditions of the Stock Purchase Agreement, at the closing of the Daré Transaction, the Selling Stockholders will collectively receive a number of shares of Cerulean common stock equal to the product of the number of shares of Daré stock held by such Selling Stockholder multiplied by an exchange ratio calculated based on the relative valuations of each of Daré and Cerulean at the closing of the Daré Transaction. Also in connection with the Daré Transaction, Cerulean will assume the (i) outstanding stock option awards of Daré, and (ii) outstanding warrants of Daré, each of which will be adjusted to reflect the exchange ratio for the Daré Transaction. Immediately following the closing of the Daré Transaction, we expect that the Selling Stockholders will own between approximately 51% and 70% (depending on the net cash positions of us and Daré at closing) of the outstanding equity securities of Cerulean Pharma Inc.

Consummation of the Daré Transaction is subject to certain closing conditions, including, among others, (1) approval of the issuance of the shares of our common stock in the Daré Transaction by our stockholders in accordance with applicable NASDAQ Stock Market, Inc., or NASDAQ, rules, which (assuming a quorum is present) require the affirmative vote of a majority of the shares of our common stock, present in person or represented by proxy and entitled to vote on the subject matter (excluding broker non-votes and abstentions), (2) the absence of any order, executive order, stay, decree, judgment or injunction or statute, rule or regulation that makes the consummation of the Daré Transaction illegal, or otherwise prohibits the consummation of the Daré Transaction, and (3) the approval of the NASDAQ Initial Listing Application—For Companies Conducting a Business Combination that Results in a Change of Control with respect to the shares of our common stock to be issued in connection with the Daré Transaction. Each party's obligation to consummate the Daré Transaction is also subject to other specified customary conditions, including (1) the representations and warranties of the other party (with Daré and the Selling Stockholders being considered together for such purposes) being true and correct as of the date of the Stock Purchase Agreement and as of the closing date of the Daré Transaction, generally subject to an overall material adverse effect qualification, and (2) the performance in all material respects by the other party (with

Daré and the Selling Stockholders being considered together for such purposes) of its obligations under the Stock Purchase Agreement . The Stock Purchase Agreement contains certain termination rights for both us and Daré, and further provides that, upon termination of the Stock Purchase Agreement under specified circumstances, we may be required to pay Daré a termination fee of $0.3 mil lion, or Daré may be required to pay us a termination fee of $0.45 million. There can be no assurances that the Daré Transaction will be consummated.

On March 19, 2017, we also entered into an asset purchase agreement, or the Novartis Asset Purchase Agreement, with N ovartis Institutes for BioMedical Research, Inc., or Novartis . Under the Novartis Asset Purchase Agreement we agreed to sell and assign to Novartis all of our right, title and interest in and to the patent rights, know-how and third-party license agreements relating to the Platform. We also agreed to transfer and assign to Novartis any agreements that we have with third parties conducting research, development, or manufacturing activities with the Platform. We refer to this transaction as the Novartis Transaction. At the closing of the Novartis Transaction, Novartis will be obligated to pay us a purchase price of $6.0 million.

Consummation of the Novartis Transaction is subject to us obtaining, pursuant to Delaware law, the approval of the holders of at least a majority of our common stock for the sale of substantially all of its assets in the Novartis Transaction. Each party's obligation to consummate the Novartis Transaction is also subject to other specified customary conditions, including (1) the representations and warranties of the other party being true and correct as of the closing date of the Novartis Transaction, generally subject in the case of Novartis' representations and warranties to an overall materiality qualification, and (2) the performance in all material respects by the other party of its obligations under the Novartis Asset Purchase Agreement, including in our case by obtaining all necessary corporate and third-party consents. There can be no assurances that the Novartis Transaction will be consummated.

On March 19, 2017, we also entered into an Asset Purchase Agreement with BlueLink Pharmaceuticals, Inc., or BlueLink, a subsidiary of NewLink Genetics Corporation. We refer to this as the BlueLink Asset Purchase Agreement. Under the BlueLink Asset Purchase Agreement we sold and assigned to BlueLink all of our right, title and interest in and to our clinical product candidates CRLX101 and CRLX301, or the Products. We also transferred and assigned to BlueLink the accompanying intellectual property rights and know-how to the Products. On March 21, 2017, BlueLink paid the purchase price of $1.5 million. Also in connection with the BlueLink Asset Purchase Agreement, we and BlueLink entered into a license agreement pursuant to which we granted to BlueLink an exclusive, worldwide, perpetual, sublicensable right and license, under the Platform, to research, develop and commercialize the Products. Pursuant to the Novartis Asset Purchase Agreement, Novartis will assume this license agreement upon the closing of the Novartis Transaction.

We refer to the Daré Transaction, the Novartis Transaction and the BlueLink Asset Purchase Agreement as the 2017 Strategic Transactions.

We entered into a payoff letter dated as of March 17, 2017, with Hercules Capital, Inc. (formerly known as Hercules Technology Growth Capital, Inc.), or Hercules, pursuant to which we agreed to pay off and thereby terminate our Loan and Security Agreement dated as of January 8, 2015, or the Hercules Loan Agreement, with Hercules as lender. Pursuant to the payoff letter, we paid, on March 20, 2017, a total of $12.4 million to Hercules, representing the principal, accrued and unpaid interest, fees, costs and expenses outstanding under the Hercules Loan Agreement in repayment of our outstanding obligations under the Hercules Loan Agreement. This payoff amount included a final end of term charge to Hercules in the amount of $1.4 million, representing 6.7% of the aggregate original principal amount advanced by Hercules. Upon the payment of the $12.4 million pursuant to the payoff letter, all outstanding indebtedness and obligations to Hercules under the Hercules Loan Agreement were deemed paid in full, and the Hercules Loan Agreement was terminated.

On March 20, 2017, we announced a restructuring including the elimination of approximately 58% of our workforce, to a total of eight full-time equivalent employees, under a plan expected to be completed during the second quarter of 2017.

Overview

The Platform is designed to create nanoparticle-drug conjugates, or NDCs, with the aim of providing safer and more effective therapies for patients living with cancer. NDCs consist of anti-cancer therapeutics, or payloads, covalently linked to a proprietary polymer. An important goal for all drugs is to maximize the net clinical benefit by increasing the desired therapeutic effect while reducing adverse effects. This is especially difficult with drugs used to treat cancer, where the goal is to destroy or inhibit growth of cancer cells without damaging healthy cells. We believe NDCs concentrate their anti-cancer payloads inside tumor cells while sparing normal tissue because they are small enough to pass through the leaky pores of new blood vessels in tumors as an entry portal into tumor tissue, but are too large to pass through the pores of healthy blood vessels. Once inside tumors, we believe NDCs are actively taken up into tumor cells where they slowly release their anti-cancer payloads, providing a durable inhibition of their targets.

Based on their properties and design, NDCs have the potential to enable synergistic combination therapies that can offer better tolerability and efficacy. We believe that better tolerability can be achieved through the preferential accumulation of the NDC in the

tumor cells while better efficacy can be achieved by combining drugs that have different and complementary mechanisms of action. Cancer is a multi-faceted disease that is rarely adequately addressed by one therapy. Tumor cells are genetically div erse and can rapidly resist and ultimately overcome a single-agent therapy by modulating various adaptive pathways; however, if multiple drugs simultaneously shut down multiple adaptive pathways, there is a greater chance of achieving favorable disease res ponses for an extended period of time.

The Platform generated two clinical-stage NDCs. The first clinical candidate generated by the Platform, CRLX101, is an NDC with a camptothecin payload. Camptothecin is a potent topoisomerase 1, or topo 1, inhibitor that was too toxic to develop in the clinic; however, CRLX101 reduces the toxicities associated with this highly potent agent, while increasing the payload concentration in tumors. The second clinical candidate generated by the Platform, CRLX301, is an NDC with a docetaxel payload. Docetaxel is a commercially successful oncology drug that suffers from significant toxicities. We sold both clinical candidates to BlueLink on March 19, 2017.

In August 2016, we announced top-line results from our Phase 2, randomized, multi-center clinical trial of CRLX101 in combination with Avastin in the treatment of patients with advanced renal cell carcinoma, or RCC. We refer to this trial as the RCC Trial. The RCC Trial was conducted at 43 sites in the United States and South Korea, and enrolled 115 patients with RCC who progressed through two or three prior lines of therapy. Patients were randomized to receive CRLX101 in combination with Avastin or investigator's choice standard of care, or SOC, therapy. The primary endpoint was progression free survival, or PFS, in the clear cell population assessed by independent radiological review. Secondary endpoints included overall response rate, duration of response and overall survival. The study demonstrated no statistically significant difference in median PFS and objective response rate for the CRLX101 and Avastin combination compared to SOC. The CRLX101 and Avastin combination appeared to be safe and well-tolerated and the safety and tolerability profile of the combination was consistent with that observed in previous studies. We presented the full data set from the RCC Trial at the Fifteenth International Kidney Cancer Symposium in November 2016. Based on these top-line results, we submitted a letter to the FDA voluntarily surrendering the Fast Track Designation in metastatic RCC we received in April 2015. We discontinued development of CRLX101 in this indication.

Following the announcement of the RCC Trial data, we announced in August 2016 that our board of directors approved a plan to reduce the size of our workforce by approximately 48% to a total of 23 full-time equivalent employees. The workforce reduction, which was substantially completed in December 2016, was designed to reduce our operating expenses while we conducted a review of development options for CRLX101. As of December 31, 2016, we had 19 full-time employees.

The Platform: Dynamically Tumor Targeted NDCs

The Platform has the potential to create additional NDCs for development by us or in collaboration with our partners. For example, in October 2016 we announced a collaboration with Novartis pursuant to which we are to create NDC candidates using the Platform and Novartis-selected active pharmaceutical ingredients, and Novartis will be responsible for the development and commercialization of NDC product candidates resulting from our collaborative research efforts. The initial research term of the collaboration agreement is two years, which can be extended for up to two additional one-year terms. We received a $5.0 million upfront payment under the collaboration agreement, and are entitled to receive additional research, development, regulatory and sales milestone payments, as well as royalties on net sales of any NDC product commercialized by Novartis. In addition, we are entitled to receive funding for up to five full-time employees to be engaged in activities under the collaboration during the research term. If the Novartis Transaction is consummated, this collaboration agreement will be superseded by the Novartis Asset Purchase Agreement.

Our Corporate Strategy

Prior to the 2017 Strategic Transactions, our goal had been to leverage our Platform to discover, develop and commercialize NDCs for the treatment of patients with inadequately treated diseases. In view of the closing of our sale of our key clinical assets pursuant to the BlueLink Asset Purchase Agreement, our goa l is to consummate the Daré Transaction and the Novartis Transaction, each of which is subject to stockholder approval. More specifically:

- If our stockholders approve both transactions, all other applicable closing conditions are satisfied or waived and both transactions are consummated, Novartis would purchase our Platform for $6.0 million and our stockholders from prior to the Daré Transaction would hold a minority equity position in Cerulean following the Daré Transaction, which we expect would be betwee n approximately 30% and 49% (depending on the net cash positions of us and Daré at closing) of the outstanding equity securities of Cerulean.
- I f our stockholders approve the Daré Transaction but do not approve the Novartis Transaction:
    - we would likely not be able to sell our Platform prior to the closing of the Daré Transaction and the percentage of our outstanding equity securities to be held following the consummation of the Daré Transaction by our

stockholders prior to the Daré Transaction would likely b e reduced as a result of our having less cash on hand at the closing of the Daré Transaction; and

- Cerulean would continue to own, following the Daré Transaction, the Platform technology, subject to the currently existing Novartis collaboration, and the board, in consultation with the management team, will make a determination regarding further exploitation of these rights; and
- If we attempt to sell the Platform to another third party or if our board decides to continue operating the Platform, Novartis may exercise its termination rights under the currently existing collaboration agreement.

- I f our stockholders do not approve the Daré Transaction, then our stockholders will continue to hold their current equity in Cerulean and our board will make a determinati on at that time concerning the future course of our company, which could include the wind-down of Cerulean and the distribution of its assets to stockholders. If our stockholders approve, and we are able to consummate, the Novartis Transaction, the purchase price of $6.0 million could increase the assets available for distribution to our stockholders in any such wind-down and liquidation.

Our Product Pipeline

We currently do not have any product candidates in development. In March 2017, we sold CRLX101 and CRLX301 to BlueLink.

Our Collaborators

A key component to our strategy is to collaborate with other companies to discover and develop new NDCs using the Platform. In October 2016 we announced a research collaboration with Novartis pursuant to which we are to create NDC candidates using the Platform and Novartis-selected active pharmaceutical ingredients. If the Novartis Transaction is consummated, this collaboration agreement will be superseded by the Novartis Asset Purchase Agreement.

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 may successfully develop and commercialize would 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.

Companies with marketed nanotechnology-based oncology products include Celgene Corporation (Abraxane® (nab-paclitaxel) indicated for breast cancer, NSCLC and pancreatic cancer), Janssen Products, LP (Doxil indicated for ovarian cancer and, in combination with Velcade ® (bortezomib), for multiple myeloma), Merrimack Pharmaceuticals, Inc. (Onivyde ™ (irinotecan liposome injection) indicated for pancreatic and colorectal cancer) and Spectrum Pharmaceuticals, Inc. (Marqibo® (vincristine sulfate liposome injection) indicated for relapsed Philadelphia chromosome-negative acute lymphoblastic leukemia). Companies with nanotechnology-based oncology product candidates in clinical development include, without limitation, BlueLink (a wholly owned subsidiary of NewLink Genetics Corporation, now developing CRLX101 and CRLX301), 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), Cristal Delivery B.V. d/b/a Cristal Therapeutics (CriPec® docetaxel for oncology), Nektar Therapeutics (NKTR102 for solid tumors), Nippon Kayku Seizo Co., Ltd. (NK105 in breast cancer), Starpharma Holdings Ltd. (DEP® docetaxel for oncology), and Supratek Pharma Inc. (SP1049C for solid tumors).

The key competitive factors affecting the success of any therapeutic product candidates that we may develop, 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 that we may use to generate product candidates, 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 also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen, and maintain our proprietary positions.

If we are unable to consummate the Novartis Transaction and/or the Daré Transaction, we may continue to expand our intellectual property estate by filing patent applications directed to improvements of the Platform as well as dosage forms, methods of treatment and additional compositions created or identified from the Platform and development of any product candidate we may choose to develop. In such event, our success would 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.

Patents

Prior to entering into the 2017 Strategic Transactions, our patent portfolio included issued patents and pending applications worldwide. These patents and applications fell into three broad categories: (1) NDCs comprising covalent linkage of specific therapeutic agents to our proprietary cyclodextrin polyethylene polymer, or CDP, including without limitation CRLX101 and CRLX301; (2) methods of use of our NDCs, including without limitation CRLX1 01 and CRLX301; and (3) our evolving Platform relating to polymeric NDCs. We held issued patents in the United States, Japan, and several other countries, covering the Platform and the conjugation of our proprietary polymer using linkers to a variety of th erapeutic agents (including without limitation CRLX101 and CRLX301), that expire in 2023 and 2024, excluding any potential patent term extension.

Pursuant to the BlueLink Asset Purchase Agreement, we sold our patent families relating specifically and solely to composition of matter and/or methods of use of CRLX101 and CRLX301 to BlueLink and granted to BlueLink an exclusive, worldwide, perpetual, sublicensable right and license, under the Platform, to research, develop and commercialize CRLX101 and CRLX301.

If the Novartis Transaction is consummated, (1) our patents relating to the covalent linkage of specific therapeutic agents to our CDP (including specific claims relating to the composition of matter of CRLX101), methods of use of NDCs generally, and the Platform generally will be sold to Novartis, and (2) Novartis will assume the license agreement to BlueLink relating to the Platform. Upon the consummation of the Novartis Agreement, we will have sold all of the company's intellectual property rights.

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 United States Patent and Trademark Office, or 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 any pharmaceutical products we may choose to develop 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 NDCs are based on trade secrets and know-how that are not publicly disclosed. We protect tr ade 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 de veloped 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 m isappropriation 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, the Russian Federation, Singapore, Switzerland, Turkey, and Ukraine and is covered by a pending application for trademark registration in Canada. The trademark is solely owned by Cerulean Pharma Inc., in the field of pharmaceutical preparations as well as in the field of diagnostic and prognostic preparations. The Cerulean logo is a registered trademark in the United States and is solely owned by Cerulean Pharma Inc. CERULEAN with the Cerulean logo is a registered trademark in Mexico and is solely owned by Cerulean Pharma Inc. The term "Leadership in Nanopharmaceuticals" is a registered trademark in the United States and is solely owned by Cerulean Pharma Inc. The symbol ™ indicates an unregistered 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 Pharmaceuticals, Inc., or 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.

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 wh ether 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 lat er 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 a re 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 t he 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.

If the Novartis Transaction is consummated, the CRLX101 Agreement will be assigned to Novartis. Pursuant to the BlueLink Asset Purchase Agreement, BlueLink will be responsible for the continued development of CRLX101 and the payment of further milestones and royalties, as described above.

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.

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 December 2014, we made a milestone payment of $250,000 to Calando in January 2015. 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.

If the Novartis Transaction is consummated, the Platform Agreement will be assigned to Novartis. Pursuant to the BlueLink Asset Purchase Agreement, BlueLink will be responsible for the continued development of CRLX301 and the payment of further milestones and royalties, as described above.

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 originally 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.

If the Novartis Transaction is consummated, the Caltech licensed patent rights will be assigned to Novartis. Pursuant to the BlueLink Asset Purchase Agreement, BlueLink will be responsible for the continued development of CRLX101 and CRLX301 and the payment of royalties as described above.

Manufacturing

We have contracted with third parties for the manufacture of NDCs for preclinical studies and clinical trials and may continue to do so in the future. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of NDCs. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities.

The manufacture of NDCs requires the manufacture of complicated polymer backbone structures as well as therapeutic agents. Although these characteristics may limit alternative third party manufacturers, we believe that there are several sources of supply that can satisfy clinical and commercial requirements, including back-up suppliers for certain stages of the manufacturing process. We cannot be certain, however, that identifying and establishing relationships with secondary sources, if necessary, would not result in significant delay or material additional costs.

Sales and Marketing

We have no current plans to build the commercial infrastructure in the United States necessary to effectively support the commercialization of any NDCs we may develop in the future, if approved.

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 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 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;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- 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 United States. 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 act ions 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 st udies 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.

Phase 4. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

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. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA or the sponsor or the data monitoring committee 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. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

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 FDA'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 s ponsor 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, or ISTs, 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 ISTs, 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.

The terms of IST agreements customarily 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 or licenses to us all intellectual property rights relating to the drug, (c) we are responsible for supplying the 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 $2.03 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $97,000 per product and $510,000 per establishment for fiscal year 2017. Important exceptions or waivers for user fees include:

- A small company (fewer than 500 employees, including employees of 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 ot her 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 U.S. regulations as the sponsor.

In addition, as a condition of approval, the FDA may require an applicant to develop 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 may 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, Priority Review and Regenerative Advanced Therapy Designations

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 referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

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

Second, a product may be designated as a Breakthrough Therapy if it is intended, e ither alone or in combination with one or more other products, 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 o r more clinically significant endpoints, such as substantial treatment effects observed early in clinical development . The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product

sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross -disciplinary project lead for the review team; and taking other steps to design the clin ical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product 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 product 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 product 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.

Finally, with passage of the 21st Century Cures Act ("Cu res Act") in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to tr eat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanc ed therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies , potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

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 deficiencie s 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 applic ation does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may impose post-marketing requirements, which are studies and clinical trials that the sponsor is required to conduct under one or more statutes or regulations, or post-marketing commitments which are studies or clinical trials that the sponsor has agreed to conduct, but that are not required by a statute or regulation. The FDA may limit the approved indications for use for the product, require that contraindications, warnings and/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 Maintenance

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, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of

drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical produ ct samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Section 505(b)(2) NDAs

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

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

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. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE 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 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. Three year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five year NCE exclusivity, an award of three year exclusivity does not block the FDA from accepting ANDAs seeking

approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about award s of data exclusivity shortly before a product is approved.

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.

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. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) 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 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 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 attachme nt 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 pediat ric 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 e xtended 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.

The 21 st Century Cures Act

On December 13, 2016, President Obama signed the 21st Century Cures Act, or Cures Act, into law. The Cures Act is designed to modernize and personalize healthcare, sp ur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the National Institutes of Health. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Hea lth Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review v oucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the F DCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antib iotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

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.

Clinical Trial Approval in the European Union (EU)

Pursuant to the currently applicable Clinical Trials Directives, an applicant must obtain approval from the competent national authority of the EU member state in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU member states, the competent authorities in each of these EU member states must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. In April 2014, the EU adopted a new Clinical Trials Regulation, which replaced the Clinical Trials Directive. The new Clinical Trials Regulation is directly applicable to and binding in all 28 EU member states without the need for any national implementing legislation, and (subject to certain exceptions) became applicable in May 2016 to clinical trial applications submitted as of that time. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU member state through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU member state or in more than one EU member state. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Marketing Authorization

To obtain marketing approval of a drug under EU 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 as sessment of modifications or extensions to an existing marketing authorization.

Data and Market Exclusivity in the EU

In the EU, 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 EU 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.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom (U.K.) voted in favor of leaving the European Union (commonly referred to as "Brexit"). The withdrawal of the U.K. from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the U.K. provides a notice of withdrawal pursuant to the E.U. Treaty. The U.K. Prime Minister has stated that notice of withdrawal will be given by the end of March 2017. Since the regulatory framework for pharmaceutical products in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directive s and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the U.K. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the U.K.

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 EU 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 EU 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. EU 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.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of ph armaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States

In March 2010, the United States Congress enacted the Affordable Care Act, or ACA, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;

- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implante d or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; 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.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unabl e to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken . In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The new Administration and Congress have expressed interest in repealing and replacing certain provisions of the ACA. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. The Budget Resolution is not a law, however. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

In March 2017, the House considered new legislation to repeal and replace the ACA. That bill, however, was withdrawn when it became clear that there were not enough votes to pass it. While the President and congressional leaders have indicated that they plan to address other legislative initiatives, th ey may continue to have interest in repealing certain ACA provisions and replacing them with alternatives that may be less costly and provide state Medicaid programs and private health plans more flexibility. As a result, while it remains unclear whether new legislation will be adopted to repeal and replace the ACA, it is possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could be repealed along with ACA coverage expansion provisions if new legislation is enacted.

Employees

In March 2017, we implemented a workforce reduction of approximately 58%, affecting 11 of our current employees. We anticipate that this workforce reduction will be completed in the second quarter of 2017. As of March 30, 2017, we had 19 full-time employees, including a total of 8 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. Upon completion of our March 2017 workforce reduction, we will have no more than eight full-time employees.

Available Information

We file reports and other information with the Securities and Exchange Commission, or SEC, as required by the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov.

Our Internet website is http://www.ceruleanrx.com. We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors," as a source of information about us.

The foregoing references to our website are not int ended to, nor shall they be deemed to, incorporate information on our website into this Annual Report on Form 10-K by reference.

Item 1A. R isk 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 Securities and Exchange Commission, or SEC, press releases, communications with investors and oral statements. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Risks Related to our Proposed Transaction with Daré

Our strategic transaction with Daré may not be consummated or may not deliver the anticipated benefits we expect.

In February 2017, we announced that our board of directors had initiated a review of strategic alternatives that could result in changes to our business strategy and future operations. As part of this process, our board determined to review alternatives with the goal of maximizing stockholder value, including potentially a sale of the company, a reverse merger, a business combination or a sale, license or other disposition of company assets, and liquidation of our company. As part of this process, in March 2017, we enter ed into a stock purchase agreement, or the Stock Purchase Agreement, with Daré Bioscience , Inc., or Daré, and the holders of capital stock and securities convertible into capital stock of Daré named therein, or the Selling Stockholders, pursuant to which, among other things, the Selling Stockholders agreed to sell to us, and we agreed to purchase from the Selling Stockholders , all of the outstanding shares of capital stock, including those issuable upon conversion of convertible securities, of Daré. We refe r to this transaction as the Daré Transaction. Subject to the terms and conditions of the Stock Purchase Agreement, at the closing of the Daré Transaction, the Selling Stockholders will collectively receive a number of shares of Cerulean common stock equal to the product of the number of shares of Daré stock held by such Selling Stockholder multiplied by an exchange ratio calculated based on the relative valuations of each of Daré and Cerulean at the closing of the Daré Transaction. Also in connection with the Daré Transaction, Cerulean will assume the (i) outstanding stock option awards of Daré, and (ii) outstanding warrants of Daré, each of which will be adjusted to reflect the exchange ratio for the Daré Transaction. Immediately following the closing of t he Daré Transaction, we expect that the Selling Stockholders will own between approximately 51% and 70% (depending on the net cash positions of us and Daré at closing) of the outstanding equity securities of Cerulean Pharma Inc.

We are devoting a signific ant proportion of our time and resources to consummating this transaction, however, there can be no assurance that such activities will result in such consummation . Consummation of the Daré Transaction is subject to certain closing conditions, including, among others, (1) approval of the issuance of the shares of our common stock in the Daré Transaction by our stockholders in accordance with applicable NASDAQ Stock Market, Inc., or NASDAQ, rules, which (assuming a quorum is present) require the affirmative vote of a majority of the shares of our common stock, present in person or represented by proxy and entitled to vote on the subject matter (excluding broker non-votes and abstentions); (2) the absence of any order, executive order, stay, decree, judgment or injunction or statute, rule or regulation that makes the consummation of the Daré Transaction illegal, or otherwise prohibits the consummation of the Daré Transaction, and (3) the approval of the NASDAQ Initial Listing Application—For Companies Conducti ng a Business Combination that Results in a Change of Control with respect to the shares of our common stock to be issued in connection with the Daré Transaction. Each party's obligation to consummate the Daré Transaction is also subject to other specified customary conditions, including (1) the representations and warranties of the other party (with Daré and the Selling Stockholders being considered together for such purposes) being true and correct as of the date of the Stock Purchase Agreement and as of the closing date of the Daré Transaction, generally subject to an overall material adverse effect qualification, and (2) the performance in all material respects by the other party (with Daré and the Selling Stockholders being considered together for such purposes) of its obligations under the Stock Purchase Agreement. In the event that any of these closing conditions is not satisfied, we may not be able to consummate the Daré Transaction. In addition, even if we are able to consummate the Daré Transaction, such transaction may not deliver the benefits we anticipate or enhance stockholder value.

Certain provisions of the Stock Purchase Agreement may discourage third parties from submitting alternative acquisition proposals, including proposals that may be superior to the arrangements contemplated by the Stock Purchase Agreement.

The terms of the Stock Purchase Agreement prohibit each of us and Daré from soliciting alternative takeover proposals or cooperating with persons making unsolicited takeover propo sals, except in limited circumstances, including when such party's board of directors determines in good faith that an unsolicited alternative takeover proposal is a superior takeover proposal and is reasonably capable of being consummated. In addition, if the Stock Purchase Agreement is terminated by us or Daré under certain circumstances, including because of a decision of our board of directors to recommend a superior proposal, we would be required to pay a termination fee of $300,000 to Daré. This termination fee may discourage third parties from submitting alternative takeover proposals to us or our stockholders, and may cause our board of directors to be less inclined to recommend an alternative proposal.

Potential litigation could prevent or delay th e completion of the Daré Transaction or result in the payment of damages following completion of the Daré Transaction .

We and members of our board of directors or executive officers may in the future be parties, among others, to claims and litigation related to the Daré Transaction, including putative stockholder class actions. Among other remedies, the plaintiffs in such matters could seek to enjoin the Daré Transaction. The results of complex legal proceedings are difficult to predict, and could delay or prevent the Daré Transaction from being completed in a timely manner or at all. In addition, the existence or threat of litigation relating to the Daré Transaction could impact the likelihood of obtaining approval from our stockholders of the Daré Transaction. Moreover, any future litigation could be time consuming and expensive, could divert our attention away from regular business, and, if any potential lawsuit is adversely resolved, could have a material adverse effect on our results of operations and financial condition.

One of the conditions to the closing of the Daré Transaction is that no applicable governmental entity shall have enacted, issued, promulgated, enforced or entered any order, executive order, stay, decree, judgment or injunction (preliminary or permanent) or statute, rule or regulation which is in effect and which has the effect of making the Daré Transaction illegal or otherwise prohibiting consummation of the Daré Transaction. Consequently, if a settlement or other resolution is not rea ched in any potential lawsuit and the plaintiffs secure injunctive or other relief prohibiting, delaying or otherwise adversely affecting Daré's and/ or our ability to complete the Daré Transaction, such injunctive or other relief may prevent the Daré Transaction from being completed in a timely manner, or at all.

The announcement and pendency of the Daré Transaction, whether or not consummated, may adversely affect the trading price of our common stock and our business prospects.

The announcement and pendency of the Daré Transaction, whether or not consummated, may adversely affect the trading price of our common stock and our business prospects. For example, the closing price of our common stock as reported by NASDAQ Global Market on March 17, 2017, prior to our announcement of the Daré Transaction, was $3.32 per share, and the closing price of our common stock as reported by the NASDAQ Global Market on March 30, 2017 was $0.84 per share. This decline may be attributable in part to such announcement. In the event that the Daré Transaction is not completed, the announcement of the termination of the Stock Purchase Agreement may also adversely affect the trading price of our common stock and our business prospects.

Failure to consummate the Daré Transaction may result in us paying a termination fee to Daré and could harm our common stock price and our future business and operations.

The Daré Transaction will not be consummate d if the conditions precedent to the consummation of the transaction are not satisfied or waived, or if the Stock Purchase Agreement is terminated in accordance with its terms. If the Daré Transaction is not consummated, we are subject to the following ris ks, among others:

- if the Stock Purchase Agreement is terminated under certain circumstances, we will be required to pay Daré a termination fee of $300,000;
- the price of our common stock may decline and remain volatile ; and
- we may have insufficient assets to continue operating our business or remain solvent and could be forced to dissolve our company and liquidate our assets to pursue a dissolution and liquidation.

If the Daré Transaction does not close for any reason, our board of directors may elect to, a mong other things, attempt to complete another strategic transaction, attempt to sell or otherwise dispose of our various assets or dissolve our company and liquidate our assets. If we seek another strategic transaction or attempt to sell or otherwise dispose of our various assets, there is no assurance that we will be able to do so, that the terms would be equal to or superior to the terms of the Daré Transaction or as to the timing of such transaction. If we decide to dissolve and liquidate our assets, we would be required to pay all of our debts and contractual obligations, and to set aside certain reserves for potential future claims, and there can be no assurance as to the amount or timing of available cash left to distribute to stockholders after paying our debts and other obligations and setting aside funds for reserves.

If we do not successfully consummate the transaction with Daré, our board of directors may dissolve our company and liquidate our assets to pursue a dissolution and liquidation. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such transaction or liquidation.

If the Daré Transaction does not close for any reason, our board of directors may elect to, among other things, dissolve our company and liquidate our assets. If we decide to dissolve and liquidate our assets, we would be required to pay all of our debts and contractual obligations, and to set aside certain reserves for potential future claims, and there can be no assurances as to the amount or

timing of available cash left to distribute to stockholders after paying our debts and other obligations and setti ng aside funds for reserves.

In the event of a dissolution and liquidation, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such decision and, ultimately, such liquidation, since the amount of cash av ailable for distribution continues to decrease as we fund our operations in preparation for the consummation of the Daré Transaction. In addition, the amount of cash available for distribution in the event of a dissolution and liquidation will heavily depe nd on whether we consummate the sale of our Dynamic Tumor Targeting platform technology, or the Platform, to Novartis Institutes of BioMedical Research, Inc., or Novartis, in connection with which we would receive a $6.0 million purchase price. Further, t he Stock Purchase Agreement contains certain termination rights for each party, and provides that, upon termination under specified circumstances, we may be required to pay Daré a termination fee of $300,000, which would further decrease our available cash resources. If our board of directors were to approve and recommend, and our stockholders were to approve, a dissolution and liquidation, we would be required under Delaware corporate law to pay our outstanding obligations, as well as to make reasonable provision for contingent and unknown obligations, prior to making any distributions in liquidation to our stockholders. Our commitments and contingent liabilities may include (i) regulatory and clinical obligations remaining under our clinical trials; (ii) o bligations under our employment and retention agreements with certain employees ; and (iii) potential litigation against us, and other various claims and legal actions arising in the ordinary course of business. As a result of this requirement, a portion o f our assets may need to be reserved pending the resolution of such obligations. In addition, we may be subject to litigation or other claims related to a dissolution and liquidation of our company. If a dissolution and liquidation were pursued, our board of directors, in consultation with our advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve. Accordingly, holders of our common stock could lose all or a significant portion of their investment in the event of our liquidation, dissolution or winding up.

Risks Related to our Proposed Transaction with Novartis

Our strategic transaction with Novartis may not be consummated or may not deliver the anticipated benefits we expect.

As part of our board of directors' review of strategic alternatives, in March 2017, we entered into an asset purchase agreement, or the Novartis Asset Purchase Agreement, with Novartis, pursuant to which, among other things, we agreed to sell the Platform to Novartis. We refer to this transaction as the Novartis Transaction . At the closing of the Novartis Transaction, which requires the approval of a majority of our stockholders, Novartis will be obligated to pay a purchase price of $6.0 million.

We are devoting a significant pr oportion of our time and resources to consummating the Novartis Transaction , however, there can be no assurance that such activities will result in the consummation of this transaction. Consummation of the Novartis Transaction is subject to us obtaining, pursuant to Delaware law, the approval of the holders of at least a majority of our common stock for the sale of substantially all of our assets in the Novartis Transaction. Each party's obligation to consummate the Novartis Transaction is also subject to other specified customary conditions, including (1) the representations and warranties of the other party being true and correct as of the closing date of the Novartis Transaction, generally subject in the case of Novartis' representations and warranties to an overall materiality qualification, and (2) the performance in all material respects by the other party of its obligations under the Novartis Asset Purchase Agreement, including in our case by obtaining all necessary corporate and third-party consents . In the event that any of these closing conditions is not satisfied , we may not be able to consummate the Novartis Transaction. In addition, even if we are able to consummate the Novartis Transaction, such transaction may not deliver the benefits we anticipate or enhance stockholder value.

Potential litigation filed against us could prevent or delay the completion of the Novartis Transaction or result in the payment of damages following completion of the Novartis Transaction.

We and members of our board o f directors or executive officers may in the future be parties, among others, to claims and litigation related to the Novartis Transaction, including putative stockholder class actions. Among other remedies, the plaintiffs in such matters could seek to enjoin the Novartis Transaction. The results of complex legal proceedings are difficult to predict, and could delay or prevent the Novartis Transaction from being completed in a timely manner or at all. In addition, the existence or threat of litigation relating to the Novartis Transaction could impact the likelihood of obtaining approval from our stockholders of the Novartis Transaction. Moreover, any future litigation could be time consuming and expensive, could divert our attention away from regular business, and, if any potential lawsuit is adversely resolved, could have a material adverse effect on our results of operations and financial condition.

One of the conditions to the closing of the Novartis Transaction is that the consummation of the Novartis Tra nsaction not violate any applicable national, supranational, federal, state, local, or foreign law, statute, ordinance, principle of common law, or any rule, regulation, standard, judgment, order, writ, injunction, decree, arbitration award, agency requirement, license, or permit of any

governmental authority. Consequently, if a settlement or other resolution is not reached in any potential lawsuit and the plaintiffs secure injunctive or other relief prohibiting, delaying or otherwise adversely affecting No vartis' and/or our ability to complete the Novartis Transaction, such injunctive or other relief may prevent the Novartis Transaction from being completed in a timely manner, or at all.

The announcement and pendency of the Novartis Transaction, whether or not consummated, may adversely affect the trading price of our common stock and our business prospects.

The announcement and pendency of the Novartis Transaction, whether or not consummated, may adversely affect the trading price of our common stock and our business prospects. For example, the closing price of our common stock as reported by NASDAQ Global Market on March 17, 2017, prior to our announcement of the Daré Transaction, was $3.32 per share, and the closing price of our common stock as reported by the NASDAQ Global Market on March 30, 2017 was $0.84 per share. This decline may be attributable in part to such announcement. In the event that the Novartis Transaction is not completed, the announcement of the termination of the Novartis Asset Purchase Agreement may also adversely affect the trading price of our common stock and our business prospects.

Failure to consummate the Novartis Transaction could harm our common stock price and our future business and operations.

The Novartis Transaction will not be consummated if the conditions precedent to the consummation of the transaction are not satisfied or waived, or if the Novartis Asset Purchase Agreement is terminated in accordance with its terms. If the Novartis Transaction is not consummated, th e price of our common stock may decline and remain volatile. Additionally, if the Novartis Transaction is not consummated, our ability to consummate the Daré Transaction could be put at risk or, in the event we are nonetheless able to consummate the Daré Transaction, our stockholders may own less of the resulting company after consummation of the Daré Transaction.

Furthermore, if the Novartis Transaction does not close for any reason, our board of directors may elect to, among other things, attempt to comp lete another strategic transaction, attempt to sell or otherwise dispose of the Platform, attempt to continue the currently existing research collaboration with Novartis, seek to continue to operate the Platform or dissolve our company and liquidate our assets. If we seek another strategic transaction or attempt to sell or otherwise dispose of the Platform, there is no assurance that we will be able to do so, that the terms would be equal to or superior to the terms of the Novartis Transaction or as to the timing of such transaction. If we attempt to continue the currently existing research collaboration with Novartis, Novartis may elect to exercise its termination rights thereunder. If we decide to dissolve and liquidate our assets, we would be required to pay all of our debts and contractual obligations, and to set aside certain reserves for potential future claims, and there can be no assurance as to the amount or timing of available cash left to distribute to stockholders after paying our debts and other obligations and setting aside funds for reserves.

If we were to seek to continue to operate the Platform, we would need to determine whether and how to continue discovery and research programs. We would also need to raise funds to support continued operat ions, which we may be unable to do in a timely fashion, upon attractive terms, or at all, and re-assess our workforce requirements in consideration of our previously announced reduction in force.

Risks Related to the Operation of Our Business Without Consummation of the Daré Transaction and/or the Novartis Transaction.

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 research and development programs or commercialization efforts.

We will need to raise additional capital to fund any continued research or development programs using the Platform. As a result of our reduction in force and other cost control measures, we expect our expenses to decrease in the short term. In the future, however, we expect that our expenses may increase in connection with our ongoing activities, particularly if we continue research and development and initiate any clinical trials of, and seek regulatory approval for nanoparticle-drug conjugates, or NDCs generated through use of the Platform. In addition, if we obtain regulatory approval for any of our NDCs, 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 NDC that receives marketing approval may be substantial, and manufacturing our NDCs for commercial sale will require expensive and specialized facilities, processes and materials. Accordingly we will need to obtain substantial additional funding to advance the research and development of any NDC and to fund our continuing operations. We may

be unable to raise capital when needed or on attractive terms, and if so we could be forced to delay, reduce or eliminate any research and development programs.

In October 2016, we entered into a common stock purchase agreement with Aspire Capital Fund, LLC, or Aspire, pursuant to which Cerulean has the right to sell certain amounts of its common stock, up to an aggregate total of $20.0 million of our common stock, over a 24-month period, at prices based on a formula linked to current market prices at the time of each sale. We refer to this as the ATM. In connection with entry into the ATM, we issued 700,000 shares of our common stock to Aspire as a commitment fee, and sold 800,000 shares of our common stock at $1.25 per share, for an initial amount of $1.0 million. Up to $19.0 million remains available under the ATM, upon the terms and subject to the conditions and limitations set forth therein. While we have the right to determine the amounts and timing of sales of common stock to Aspire under the ATM, these rights are subject to certain limits and restrictions. These limits and restrictions include limits on the number of shares we can sell to Aspire on any one trading day, as well as stock price trading price restrictions, which prohibit us from making certain sales to Aspire on any trading day on which the closing sale price of our common stock is below $0.50 per share and from making any sales to Aspire on any trading on which the closing sale price is less than $0.25 per share. Accordingly, we may not be able to sell shares under the agreement at prices that we deem acceptable, and there can be no assurance that we will be able to sell the remaining $19.0 million of common stock contemplated under the ATM.

As of December 31, 2016, we had cash and cash equivalents of $35.0 million. We have no other sources of significant liquidity in place as of December 31, 2016. We expect that our existing cash and cash equivalents will fund our operations into the second half of 2017 based on our 2017 operating plan. We have undertaken a strategic review of potential financing alternatives such as the sale of the company, a merger, a business combination, a strategic investment into the company, or a sale, license or disposition of our assets. Our recurring use of cash to fund operations in combination with our rate of expenditures with no known probable source of capital raises substantial doubt about our ability to continue as a going concern. If we are unable to obtain additional funding on a timely basis, we may be required to curtail or terminate research and development activities under our collaboration agreement with Novartis, or to scale back, suspend or terminate our business operations.

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

- the number and development requirements of the NDCs we or any collaborators pursue;
- the scope, progress, timing, results and costs of researching and developing NDCs, and conducting preclinical studies and clinical trials;
- the costs, timing and outcome of regulatory review of NDCs in the United States and abroad;
- the cost and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any NDCs for which we or a collaborator receive marketing approval;
- the revenue, if any, received from commercial sales of any NDCs for which we or a collaborator 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, any product candidates we may choose to develop, if approved, may not achieve commercial success. Our commercial revenues, if any, would 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 o r require us to relinquish rights to technologies or product candidates.

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

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

Any future indebtedness could adversely affect our ability to operate our business.

Any future indebtedness, combined with current and future financial obligations and contractual commitments, 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.

Failure to make payments or comply with other covenants under any future debt instruments could result in an event of default and acceleration of amounts due. If an event of default occurs and any future lenders to us accelerate the amounts due, we may not be able to make accelerated payments, and such future lenders could seek to enforce security interests in the collateral securing such indebtedness, which could include all or substantially all of our assets.

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, 2016, we had an accumulated deficit of $200.7 million. We do not know whether or when we will become profitable. We have not generated any revenues to date from product sales and have financed our operations primarily through public offerings of our common stock, private placements of our preferred stock, convertible debt financings and secured debt financings. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- continue or start any new discovery and research programs utilizing the Platform;
- embark on new preclinical and clinical development of any NDC generated from the Platform;
- meet corresponding manufacturing, shipping and storage requirements;

- seek regulatory approvals for any NDC that successfully completes clinical trials;
- in the future, establish a sales, marketing and distribution infrastructure in the United States;
- scale up external manufacturing capabilities to commercialize any NDC for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- add equipment and physical infrastructure to support our research and development; and
- hire additional personnel and/or incur severance costs associated with the termination of employment of any existing personnel.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. We do not expect to generate significant revenue unless and until we are able to obtain marketing approval for, and successfully commercialize, one or more product candidates. This will require us to be successful in a range of challenging activities, including discovering product candidates, completing preclinical testing and clinical trials of 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 products from private insurance or government payors. We have not yet commenced most 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, or other regulatory authorities to perform studies in addition to those we may expect to conduct, or if there are any delays in completing our clinical trials or the development of any of any product candidates we may choose to develop, 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, 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.

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 managing our staffing, developing and securing our technology, raising capital and undertaking preclinical studies and clinical trials of 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 product candidates we may choose to develop, 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 Product Candidates

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

We believe that the Platform has the potential to create drugs that may have significant utility in several indications, particularly in combination with other therapies. While the results of preclinical studies and early-stage clinical trials have suggested that certain of our previous product candidates may have such utility, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any product candidate 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 product candidate known as CRLX101, which we sold to BlueLink Pharmaceuticals, Inc. in March 2017, failed to meet its primary endpoint in two randomized Phase 2 trials: a Phase 2 clinical trial of single agent CRLX101 in advanced non-small cell lung cancer, or NSCLC, for patients who had progressed through one or two prior regimens of chemotherapy, and a Phase 2 clinical trial of CRLX101 combined with Avastin (bevacizumab) in

relapsed renal cell carcinoma, or relapsed RCC, in patients who had progressed through two or three prior therapies. We refer to this latter trial as our RCC Trial.

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), Abraxane® (nab-paclitaxel), Onivyde™ (irinotecan liposomal injection) and Marqibo® (vincristine sulfate liposome injection), 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 do not currently have a lead product candidate. If we are unable to identify a product candidate to advance through research and development efforts, our business would be materially harmed.

As a result of the sale of CRLX101 and CRLX301 to BlueLink Pharmaceuticals, Inc., a wholly owned subsidiary of NewLink Genetics Corporation in March 2017, we currently have no product candidates suitable for advancing into clinical trials. If the Novartis Transaction is not consummated, and our board decides to continue operating our business based on the Platform, we will need to evaluate our NDCs to determine which, if any, are ready to move further into preclinical and clinical development. If in such event we determine that the Platform has not generated any NDCs worthy of development, our business would 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 any product candidates that we may choose to develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

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

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for any product candidates we may choose to develop, delay or halt the development of and approval processes for product candidates and jeopardize our ability to achieve 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 product candidates. Any of the foregoing could cause the value of our company to decline and limit our ability to obtain additional financing, if and when needed.

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

To obtain regulatory approval for a combination product candidate, the FDA typically requires an applicant to show that each active ingredient in an investigational combination drug candidate makes a contribution to the combined investigational drug

candidate's claimed effects and that the dosage of each component, including amount, frequency and duration, is such that the combination is safe and effective for a significant patient pop ulation requiring such concurrent therapy. This could require us to conduct more extensive and more expensive clinical trials than would be the case for a single agent pharmaceutical. As a result, the need to conduct such trials could make it more difficu lt and costly for us to obtain regulatory approval of combination drug product candidate than of a new drug containing only a single active pharmaceutical ingredient.

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

It is impossible to predict when or if any product candidate that we may choose to develop 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 would be required to complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of the 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 any product candidate that we may choose to develop would be susceptible to the risk of failure inherent at any stage of drug development, including failure to have a sufficient quantity of the product candidate available when needed, failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of severe or medically or commercially unacceptable adverse events, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable non-U.S. regulatory authority that a drug product is not approvable. It is possible that even if a product candidate has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, dose, dosing schedule, design, measurements, conduct or analysis of the applicable clinical trials. Conversely, as a result of the same factors, any clinical trials that we may conduct may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in any clinical trials that we may conduct, we may fail to detect toxicity of or intolerability caused by product candidates, or mistakenly believe that 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 the results of the Phase 1b/2 single-arm investigator sponsored trial, or IST, of CRLX101 in patients with relapsed RCC supported our hypothesis that CRLX101 in combination with Avastin may be effective in this setting, the combination of CRLX101 and Avastin failed to meet the primary endpoint in the RCC Trial. 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 with respect to any product candidates that we may choose to develop.

The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed and protocol amendments, if any, to address such flaws may not be sufficiently timely or corrective. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval.

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

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

If we experience any of a number of possible unforeseen eve nts in connection with clinical trials of any product candidate s that we may choose to develop , potential marketing approval or commercialization of those 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 any product candidate that we may choose to develop, including:

- clinical trials of the product candidate may produce unfavorable, incomplete or inconclusive results;
- we may decide, or regulators may advise us, to conduct additional clinical trials or we may decide to abandon an indication or development program following changes in the regulatory environment or competitive landscape;
- we may decide to add or to change a dosing schedule for any given clinical trial based on relevant data;
- the number of patients required for clinical trials of the product candidate may be larger than we anticipate, patient enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our supply of the product candidate may be insufficient to complete our clinical trials as planned due to a batch failure, a lack of funds, a change in priorities, planning errors or other reasons;
- our third party contractors, including those manufacturing the product candidate or components or ingredients thereof or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet our expectations in a timely manner or at all;
- we may decide to make changes to a trial protocol and fail to receive timely approval for the amendment from the applicable institutional review board(s) or ethics committee(s);
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- investigators may deviate from the trial protocol, fail to conduct the trial in accordance with regulatory requirements or misreport study data;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- prospective clinical trial sites may be unwilling to participate in one or more of our combination clinical trials due to a perceived difficulty in obtaining reimbursement from managed care plans, government, or other third party payors;
- patients who enroll in a clinical trial, or the investigators enrolling such patients, may misrepresent the patients' eligibility to participate in the trial or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the enrollment size for the clinical trial or extend the clinical trial's duration;
- for any given trial we may find it necessary to open more clinical trial sites than originally planned;
- we may have to suspend or terminate one or more clinical trials of the product candidate for various reasons, including unfavorable, incomplete or inconclusive data, unexpected delays, a change in funding priorities, a determination that the path to commercialization is too difficult or uncertain, a lack of sufficient funding, changes in the competitive or regulatory landscape, a finding that the participants are being exposed to unacceptable health risks, unexpected or serious adverse events or other unexpected characteristics of the 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 clinical trials or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;
- the FDA or comparable non-U.S. regulatory authorities may disagree with our clinical trial design or our interpretation of data from preclinical studies and clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design of our clinical trials;
- the FDA or comparable non-U.S. regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we enter into agreements for clinical and commercial supplies;

- the supply or quality of raw materials or the manufactured product candidate or drugs (whether provided by us or third parties) or other materials necessary to conduct clinical trials of the product candidate 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 any product candidates that we may choose to develop. 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 product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize 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 product candidate that we may choose to develop.

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

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

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

- foreign regulatory requirements that could burden or limit our ability to conduct our clinical trials;
- increased costs and heightened supply constraints associated with the acquisition of standard of care drugs and/or combination or comparator agents for which we may bear responsibility in certain jurisdictions;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations;
- more burdensome manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- lack of consistency in standard of care from country to country;
- diminished protection of intellectual property in some countries; and
- changes in country or regional regulatory requirements.

If clinical trials of any product candidates that we may choose to develop 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 the 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 product candid ates.

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

- be delayed in obtaining marketing approval for the 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 seek a fast track designation for product candidates that we may seek to develop. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, the FDA may still decide not to grant it. Even if we receive fast track designation, however, fast track designation does not ensure that we will receive marketing approval or that we may experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from or stated intentions of our clinical development program.

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

We may seek a breakthrough therapy designation for some product candidates that we may choose to develop. 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 a product candidate that we have chosen to develop 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 a product candidate that we choose to develop qualifies as a breakthrough therapy, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

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

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

For any product candidates that we may choose to develop that are eligible, we would plan to rely on the exclusivity period under the Orphan Drug Act to attain a competitive position. If we do not obtain orphan drug exclusivity for any drug products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition and our revenues would be reduced.

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

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

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

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

If we choose to pursue Accelerated Approval, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive such Accelerated Approval. There can be no assurance that the FDA will agree that our endpoint is an appropriate

surrogate endpoint. There can also be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for Accelerated Approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback that we will continue to pursue or apply for Accelerated Approval or any other form of exp edited 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 co uld 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 a product candidate that we may choose to develop would result in a longer time period to commercialize such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Serious adverse events of any product candidates that we may choose to develop may be identified during clinical development. Further, other unexpected properties of 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, any product candidates that we may choose to develop could cause us, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of such 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 product candidate that we may choose to develop 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 any product candidate that we may choose to develop 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.

While we believe that the Platform has the potential to improve the unfavorable adverse event profiles of multiple chemotherapeutic agents, if this hypothesis is wrong and we experience unexpected or more severe toxicities in clinical trials we conduct in the future, we may not receive approval to market, or achieve commercial success with respect to, any product candidates that we may choose to develop, which could prevent us from ever generating revenues or achieving profitability. In addition, the 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 potential product candidates.

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

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

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

Even if a product candidate that we have chosen to develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third party payor s and others in the medical community necessary for commercial success or the market opportunity for the product candidate may be smaller than we estimate.

We have never commercialized a product. Even if a product candidate that we have chosen to develop 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 product candidates may require significant resources and may not be successful. If any product candidate that we have chosen to develop 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 any such 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-, third- or later 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 any product candidates that we may choose to develop would be difficult to estimate precisely. Our estimates of the potential market opportunities would be predicated on many assumptions, including industry knowledge and publications, third party research reports and other surveys, and these assumptions would involve the exercise of significant judgment on the part of our management and would be inherently uncertain. If any of the assumptions proves to be inaccurate, the actual markets for any such product candidates could be smaller than our estimates of the potential market opportunities.

If any product candidate that we have chosen to develop 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 previou sly identified, our ability to market the drug could be compromised.

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

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

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

If we are unable to establish sales, marketing and distribution capabilities or enter into acceptable sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates that we may choose to 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 any product candidates that we may choose to develop 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 product candidates that we may choose to develop. 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 a product candidate that we may choose to develop, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product candidate independently.

We may seek one or more strategic partners for commercialization of 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 any products that we may have developed 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 product candidates that receive marketing approval.

We face subs tantial 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 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 may develop, which could render any of our potential product candidates obsolete and noncompetitive.

Companies with marketed nanotechnology-based oncology products include Celgene Corporation (Abraxane indicated for breast cancer, NSCLC and pancreatic cancer), Janssen Products, LP (Doxil indicated for ovarian cancer and, in combination with Velcade® (bortezomib), for multiple myeloma), Merrimack Pharmaceuticals, Inc. (Onivyde indicated for pancreatic cancer) and Spectrum Pharmaceuticals, Inc. (Marqibo indicated for relapsed Philadelphia chromosome-negative acute lymphoblastic leukemia). Companies with nanotechnology-based oncology product candidates in clinical development include, without limitation, BlueLink Pharmaceuticals, Inc. (wholly owned subsidiary of NewLink Genetics Corporation, now developing CRLX101 and CRLX301), Celsion Corporation (ThermoDox® (lyso-thermosensitive liposomal doxorubicin) for liver cancer and breast cancer), Cristal Delivery B.V. d/b/a Cristal Therapeutics (CriPec® docetaxel for oncology), Cytimmune Sciences, Inc. (CYT-6091 for NSCLC), Jazz Pharmaceuticals plc (which acquired Celator Pharmaceuticals, Inc. (Vyxeos™ for acute myeloid leukemia)), NanoCarrier Co., Ltd. (NC-6004 for bladder, bile duct and head and neck cancers, and NC-4016, and NC-6300 for solid tumors), NantPharma (Cynviloq™, which received fast-track designation from the FDA for breast and lung cancer), Nektar Therapeutics (OnzyealdTM for breast cancer and brain metastases), Nippon Kayku Seizo Co., Ltd. (NK105 in gastric cancer), Starpharma Holdings Ltd. (DEP® docetaxel for oncology), and Supratek Pharma Inc. (SP1049C for solid tumors).

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

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

If the FDA or comparable non-U.S. regulatory authorities approve generic versions of any products that we may develop that receive marketing approval, or such authorities do not grant such products appropriate periods of data exclusivity before approving generic versions of such products, the sales of such 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. 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 any products that we may develop may face from generic versions of such 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.

Any 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 may have intellectual property rights, including composition of matter patents, covering any product candidates that we may choose to develop, if approved, we expect that any such product candidates will compete in the same indications against other nanoparticles and delivery platforms incorporating the same generic therapeutics. In particular, if any product candidate that we may choose to develop 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 any product candidates that we may choose to develop will depend substantially, both domestically and abroad, on the extent to which the costs of such 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 such product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish and maintain pricing sufficient to realize a meaningful return on our investment.

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

Our ability to commercialize any 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 any product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us to decrease the price we might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable non-U.S. regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of

the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for any product candidate that we, or others, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any 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 any product candidates that we may choose to develop despite obtaining informed consents from our clinical trial participants. We will face an even greater risk if we commercially sell any product that we may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of any applicable product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

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

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

Risks Related to Our Dependence on Third Parties

We may rely on third parties to conduct ISTs of any future product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of any product candidates that we chose to develop may delay or impair our ability to obtain regulatory approval for such product candidates.

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

Such arrangements would provide us with certain information rights with respect to ISTs, including access to and the ability to use and reference the data resulting from the IST, including for our own regulatory filings. However, we would not control patient

enrollment in, or the quality, timing and reporting of the data from, ISTs, nor would we own the data from the ISTs. Moreover, if we were 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 any applicable product candidates. Further, if investigators or institutions were to breach their obligations with respect to the clinical development of any such product candidates, or if the data were to prove to be unfavorable, incomplete or inconclusive, then our ability to design and conduct any future clinical trials ourselves could 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 any planned trials and/or may not accept such additional data as adequate to initiate any planned trials. Moreover, there is typically no independent review of the results of ISTs. Therefore, the investigators may interpret the results of ISTs more favorably than an independent review would.

Moreover, ISTs of any product candidates that we may choose to develop 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 any such 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 may 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 may rely on third party clinical research organizations, or CROs, site management organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct future clinical trials of any product candidates that we may choose to develop. We may also rely on these third parties to collect and monitor adverse event data for clinical trials. Any agreements with these third parties would 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 the applicable product candidate to market could be delayed.

Our reliance on these third parties for research and development activities would reduce our control over these activities but would not relieve us of our responsibilities. For example, we would design our clinical trials and would 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 would not relieve us of these responsibilities and requirements. We are also required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

We also may rely on other third parties to manufacture, store and distribute drug supplies for clinical trials. Any performance failure on the part of such distributors could delay clinical development or marketing approval of any product candidates that we may choose to develop or commercialization of 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 product candidates that we may choose to develop and to leverage the Platform for our collaborators' product candidates. If such collaborations are not successful, or we fail to enter into such collaborations, we may not be able to capitalize on the market potential of any such product candidates or the Platform.

We may seek third-party collaborators for development and commercialization of product candidates that we may choose to develop or to leverage the Platform. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies,

biotechnology companies and certain governmental agencies. We will have limited control over the amount and timing of resources that any of our current or potential future collaborations dedicate to the devel opment or commercialization of product candidates that we may choose to develop or to the use of the Platform . Our ability to generate revenues from these arrangements will depend significantly on our collaborators' abilities to successfully perform the fu nctions assigned to them in these arrangements.

Collaborations involving product candidates that we may choose to develop or the Platform 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 the product candidates that we have chosen to develop or the product candidates we help them develop, or they may elect not to continue or renew research, development or commercialization programs based on preclinical or 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;
- our agreements with collaborators may block us from researching and developing product candidates for our own benefit or for the benefit of other or future collaborators;
- collaborators may not initiate clinical trials or if initiated, they may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new dosing schedule, dose level or formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with products or product candidates that we have chosen to develop if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe our intellectual property rights or the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of relevant products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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

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

The Platform, our drug development programs and the potential commercialization of any product candidates that we may choose to develop will require substantial additional cash to fund expenses and we may seek collaborations with pharmaceutical and biotechnology companies to leverage our Platform for the development and potential commercialization of product candidates.

We would face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement with a potential collaborator will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the value of the Platform and associated intellectual property rights, 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 technology platforms, 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 technology or 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-con suming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the Platform or a product candidate, reduce or delay research or relevant development programs, delay potential commercialization of product candidates 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 research, 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 research or develop product candidates or technology to bring them to market and generate product revenue.

We will need to contract with third parties for the manufacture of any future product candidates for preclinical and clinical testing and likely also for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of such 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 trial materials and have limited personnel with manufacturing experience. We will need to rely on third party contract manufacturers to manufacture supplies of any product candidates for preclinical and clinical testing, as well as for commercial manufacture if any product candidates that we may choose to develop receive marketing approval.

NDCs must be manufactured through complex, multi-step synthesis processes that are time-consuming and involve special conditions at certain stages. Drug substance manufacture requires high potency containment, and drug product manufacture requires high potency containment under aseptic conditions, also referred to as sterile manufacture. Failures in either drug substance manufacture or drug product manufacture, whether on the part of our future manufacturers or as a result of our failure to make timely and effective improvements in our manufacturing processes, could materially delay clinical development or marketing approval of any product candidates that we may choose to develop or result in our inability to generate sufficient supplies to meet clinical or commercial demands.

Typically, 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, we may 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 a 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 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 any such product candidates or products.

Any future product candidates that we may develop may compete with other product candidates and products for access to manuf acturing 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 may rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce product candidates for clinical studies. There are a small number of suppliers for certain capital equipment and raw materials that are used in the manufacture of NDCs. Such suppliers may not sell these raw materials to our manufacturers at the times we need them or on commercially reasonable terms. We may not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we may 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 clinical studies, product testing and potential regulatory approval of product candidates. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for product candidates that we have chosen to develop, the commercial launch of such 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 the product candidates.

Our anticipated future dependence upon others for the manufacture of any product candidates that we may choose to develop 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 any products that we may develop 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 any products that we may develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and any product candidates that we may choose to develop.

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 or that we develop on third parties' behalf. 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 or licensees 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 any products that we may develop, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

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

Certain aspects of the Platform technology are protected in whole or in part 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 products for which we have obtained approval will be harmed.

We are a party to several license agreements and certain aspects of the Platform depend on patents and/or patent applications owned by others. In particular, we hold exclusive licenses from Calando Pharmaceuticals, Inc., or Calando, and California Institute of Technology, or Caltech, and have been assigned certain patents from Calando for CDP-based product candidates. We may 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 product candidates could be materially harmed.

Our licensors or licensees 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 or licensees 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 NDCs and our ability to utilize the Platform are not dependent on the rights that we license from Calando, our license agreements with Calando could be rejected in connection with Calando's bankruptcy, in which case, we could, subject to elections and other rights and defenses that may be available to us, lose certain rights granted to us under such licenses. In March 2015, the bankruptcy court granted Calando's bankruptcy trustee's application to retain a broker to help sell

Calando's rights in certain assets including its rights in the license agreements with Cerulean. We reserved our rights with respect to any such sale. The bankruptcy trustee has obtained numerous extensions to the deadline to reject, as sume or assume and assign executory contracts including our license agreements. The trustee's last deadline was February 7, 2017. To our knowledge, no sale of such rights was ever consummated.

In addition, in spite of our best efforts, our licensors might conclude that we have materially breached our intellectual property agreements and might therefore terminate the intellectual property agreements, thereby removing our ability to obtain regulatory approval and to market products covered by these intellectual property agreements. If our intellectual property agreements are terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors may have the freedom to seek regulatory approval of, and to market, products similar or identical to ours. Moreover, if our intellectual property agreements are terminated, our former licensors and/or assignors may be able to prevent us from utilizing the technology covered by the licensed or assigned patents and patent applications. For example, under our agreements with Calando, which relate to the Platform and future NDCs, 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. 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 the inventions for any governmental purpose. In addition, the United States government would have 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 would also have 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 would be permitted to acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the United States government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for United States manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

Third parties may initiate legal procee dings 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 product candidates and use the Platform and any related intellectual property 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 any products that we may develop and our 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 any products that we may develop and our 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 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 potentially seeking patents for product candidates that we chose to develop, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment

agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, we face the risk of cybercrime. For instance, someone could hack our information networks and gain ill icit access to our proprietary information including our trade secrets. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Even if we are succes sful 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 sec rets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory Approval and Marketing of Any Product Candidates that We May Choose to Develop 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 any product candidates that we may choose to develop. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize such product candidates, and our ability to generate revenue will be materially impaired.

Drug 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 other similar regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. Any product candidates that we may choose to develop would be subject to the risks of failure inherent in drug development. We have not received approval to market any 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. Any product candidates that we may choose to develop 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 product candidate that we may choose to develop receives marketing approval, the accompanying label may limit the approved use of the 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 any product candidates that we may choose to develop, the commercial prospects for such product candidates may be harmed and our ability to generate revenues will be materially impaired.

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

Upon submission of an application for marketing approval in the United States, the FDA may convene an advisory committee (public or closed) to provide the FDA with independent advice from outside experts with specific questions regarding a pending review matter. The opinions or advice expressed by the advisory committee, or any voting decision, are not binding and the FDA retains the ultimate approval power over an application. Regardless of the committee meeting outcome or the FDA's final approval decision, public presentation of our data may shed positive or negative light on our application. A negative advisory committee meeting could signal a lower likelihood of approval, although the FDA may still end up approving our application. Conversely, an

oncologic drugs advisory committee, or ODAC, could vote in favor of approval and the FDA may still not approve our application. For an expedited review such as priority review, where the FDA's oncology office has moved focus to how quickly a drug might be approved and has commonly completed their review and approved products well before the P DUFA goal date, preparations for an ODAC could slow down approval. For us as the applicant, preparation time for an ODAC could take six months or more of dedicated effort by the program team, management, and consultants, in addition to supporting the FDA' s review queries or any other activities in the same timeframe, reducing resource efficiency. It should not be assumed that an application brought in front of the ODAC means that a negative decision is pending. The FDA determines whether or not to have a n ODAC meeting depending on the quality of the application, the results of the clinical trials, and whether similar issues, such as endpoints or trial designs, have been previously discussed at these meetings. The FDA has generally taken more problematic or complicated applications to an ODAC, which allows for presentation of their findings and a public discussion of issues at hand. On occasion, the FDA will convene an ODAC to have the public clearly understand their viewpoint on the particular applicatio n and its supporting evidence, or if there is a first in class or first in indication compound under review.

Failure to obtain marketing approval in foreign jurisdictions would prevent any product candidates that we may choose to develop from being marketed abroad.

In order to market and sell 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 any products we develop in any market.

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

Even if we obtain marketing approval for any product candidates that we may develop, the terms of approvals and ongoing regulation of such products may limit how we manufacture and market such 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 product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

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

Accordingly, assuming we receive marketing approval for any product candidate that we may choose to develop, 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 any future 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 mark et and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with any future 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 product candidate that we choose to develop receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

Regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA and other agencies, including the Department of Justice, closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market 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 products that we have developed, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- litigation involving patients taking such 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 the products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

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

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

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

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

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

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our financial results. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize 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 any product candidates that we may choose to develop, 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 any products that we may develop, if approved, to be cost-effective compared to other available therapies, they may not cover such 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 any products that we may develop, if approved.

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

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

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

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and

- established the Ce nter for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the gover nment to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

We expect that the ACA, 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 products.

In addition, with the new Administration and Congress, there may be additional legislative changes, including repeal and replacement of certain provisions of the ACA. It remains to be seen, however, precisely what the new legislation will provide, when it will be enacted and what impact it will have on t he availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates. For example, the President and congressional leaders have expressed interest in repealing certain ACA provisions and replacing them with alternatives that may be less costly and provide state Medicaid programs and private health plans more flexibility. It is possible that these repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance cover age or in individuals having insurance coverage with less generous benefits. The scope and likelihood of potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, however, and it is possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions.

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 any product candidates that we may seek to develop, 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 any products that we may develop, 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 the applicable product candidate to other available therapies. If reimbursement of any products that we may develop is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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

We are exposed to the risk of fraud or other misconduct by our employees or consultants, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, provide accurate information to the FDA or comparable non-U.S. regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us.

Misconduct by employees or consultants could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to o ur reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental invest igations 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 actio ns could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

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

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on Christopher Guiffre, our President and Chief Executive Officer, as well as the other members of our executive and scientific teams. The loss of any of these persons could impede the achievement of our goals. Although we have formal employment agreements with Mr. Guiffre and other officers of the company, these agreements do not prevent any one of them from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing, finance and sales and marketing personnel will also be critical to our success. The loss of the services of key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. For example, if key scientific personnel are terminated or voluntary resign, our ability to operate the Platform and generate future product candidates could be materially harmed. Furthermore, replacing executive officers and key employees, including, for example, finance and clinical personnel, may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize any product candidates we may choose to develop. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Since August 2016, we have twice reduced the size of our organization, and we may encounter difficulties in managing our business as a result of these reductions, or the attrition that may occur following these reductions, which could disrupt our operations. In addition, we may not achieve anticipated benefits and savings from these reductions.

In August 2016, we implemented a reduction in force that reduced the number of our employees by approximately 48%. In March 2017, we implemented a reduction in force that reduced the number of our employees by approximately 58%. These reductions in force resulted in the loss of employees across all functions, the loss of institutional knowledge and expertise and the reallocation

and combination of certain roles and responsibilities across our organization, all of which could adversely affect our operations. In addition, as with any reduction in force, there is a risk of reduced emp loyee morale and we may face difficulties retaining employees that we have asked to stay, which could result in further attrition.

We must continue to manage our operations and retain qualified personnel, each of which will be made more challenging by these reductions in force. As a result, our management may need to divert a disproportionate amount of its attention away from our day-to-day strategic and operational activities, and devote a substantial amount of time to managing the organizational changes brought about by these reductions in force. Due to our limited resources, we may not be able to effectively manage the changes in our business operations resulting from these reductions in force, which may result in weaknesses in our operations, risks that we may not be able to comply with legal and regulatory requirements, loss of business opportunities, loss of employees and reduced productivity among remaining employees. If our management is unable to effectively manage this transition, our expenses may be higher than expected, and we may not be able to implement our business strategy or achieve the anticipated benefits and savings from these reductions in force. We may also determine to take additional measures to reduce costs, which could result in further disruptions to our operations and present additional challenges to the effective management of our company.

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 December 31, 2016, the closing price of our common stock as reported by the NASDAQ Global Market ranged from a high of $10.66 per share to a low of $0.63 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:

- whether we are able to consummate the Daré Transaction and the Novartis Transaction;
- the results of our efforts to discover, develop, acquire or in-license product candidates or products, if any;
- failure or discontinuation of any of our research programs;
- actual or anticipated results from, and any delays in, any future clinical trials, as well as results of regulatory reviews relating to the approval of any product candidates that we may choose to develop;
- the level of expenses related to any product candidates that we may choose to develop or clinical development programs that we may choose to pursue;
- 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.

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.

If we were to be delisted from The NASDAQ Global Market, it could reduce the visibility, liquidity and price of our common stock.

There are various quantitative listing requirements for a company to remain listed on The NASDAQ Global Market, including maintaining a minimum bid price of $1.00 per share. The closing price per share of our common stock from January 1, 2017 to March 28, 2017 ranged from a high of $3.32 to a low of $0.69. If the minimum bid price of our common stock were to fall below $1.00 per share for 30 consecutive business days, we would likely receive notification from The NASDAQ Global Market that we were not in compliance with the $1.00 minimum bid price rule, in which case we could be subject to delisting from The NASDAQ Global Market if we were unable to regain compliance within a period of 180 calendar days. For example, on November 17, 2016, NASDAQ notified us that we were not in compliance with the $1.00 minimum bid price rule because the minimum bid price of our common stock fell below $1.00 for 30 consecutive days. However, on February 17, 2017, we received another notification from NASDAQ notifying us that our minimum bid deficiency had been cured because the closing bid price of our common stock had been above $1.00 for the prior 10 consecutive trading days. There is no guarantee that we will be able to continue complying with the minimum bid price rule or other NASDAQ Global Market requirements.

Delisting from the NASDAQ Global Market could reduce the visibility, liquidity and price of our common stock.

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 March 15, 2017, our executive officers and directors and their affiliates beneficially owned 18.0% of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to exert a significant degree of influence over matters submitted to our stockholders for approval, as well as our management and affairs. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire. For example, these persons, if they choose to act together, would be able to have significant influence on the election of direc tors and approval of any merger, consolidation or sale of all or substantially all of our assets, including the outcome of the anticipated stockholder votes with respect to the Daré Transaction and the Novartis Transaction. In particular, each of our dire ctors and their affiliates, holding in the aggregate approximately 18.0% of our outstanding common stock have each entered into a support agreement in favor of Cerulean in connection with the Daré Transaction

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, 2016, there were 4 , 020,288 shares subject to outstanding options. All of these shares under the Securities Act have been registered on a registration statement on Form S-8. These shares can be freely sold in the public m arket 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, 2016, there were 365,564 shares subject to outstanding warrants to purchase common stock. These shares will become eligible for sale in the public market, to the extent such warrants are exercised, as permitted by Rule 144 under the Securities Act. Moreover, holders of approximately 6.3 million shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statement s that we may file for ourselves or other stockholders.

The sale of our common stock to Aspire may cause substantial dilution to our existing stockholders and the sale of shares of our common stock acquired by Aspire could cause the price of our common stock to decline.

In October, 2016, we entered into a common stock purchase agreement with Aspire Capital Fund, LLC, or Aspire, pursuant to which we have the right to sell up to an aggregate of $20.0 million of our common stock over a 24-month period, at prices based on a formula linked to current market prices at the time of each sale. We refer to this as our ATM. As of December 31, 2016, up to $19.0 million remained available for us to sell to Aspire pursuant to the terms and conditions of the ATM. Although we have the right to control the timing and amount of sales of our shares to Aspire under the ATM, we are subject to certain restrictions, including without limitation restrictions on the number of shares we can sell to Aspire on any one trading day, as well as trading restrictions based on the price of our common stock. Accordingly, we may not be able to sell shares of our common stock to Aspire under the ATM at prices that we deem acceptable. There can be no assurance that we will be able to sell the remaining $19.0 million of common stock contemplated under the ATM.

Additionally, our sales of shares to Aspire may result in substantial dilution to the interests of other holders of our common stock, and such sales, or the anticipation of such sales, may cause the trading price of our common stock to decline. Furthermore, Aspire may sell some or all of our shares that it has purchased or may in the future purchase from us under the facility and any such sales may cause the trading price of our common stock to decline.

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

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

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

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

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder 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 subje ct 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. 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 currently consist of approximately 21,239 square feet of office and laboratory space located at 35 Gatehouse Drive, Waltham, Massachusetts, or the Lease. We amended the Lease, effective March 29, 2017, to remove 1,753 square feet from the Lease, which space was previously used for vivarium and vivarium support purposes. The Lease expires in February 2021, 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 NDCs and our ability to utilize the 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 27, 2015, the bankruptcy court granted Calando's bankruptcy trustee's application to retain a broker to help sell Calando's rights in certain assets including its rights in the license agreements with Cerulean. We reserved our rights with respect to any such sale. The trustee's last deadline was February 7, 2017. To our knowledge, no sale of such rights was ever consummated.

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

None.

P ART II

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

Market Information

Our common 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.

	Common Stock Price	
	High	Low
Fiscal year ended December 31, 2016		
First Quarter	$ 3.62	$ 1.82
Second Quarter	$ 4.33	$ 1.94
Third Quarter	$ 3.37	$ 0.92
Fourth Quarter	$ 1.20	$ 0.63
Fiscal year ended December 31, 2015		
First Quarter	$ 10.87	$ 5.68
Second Quarter	$ 9.24	$ 4.25
Third Quarter	$ 5.20	$ 2.77
Fourth Quarter	$ 4.30	$ 2.79

Holders

As of the close of business on March 1, 2017, there were approximately 38 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

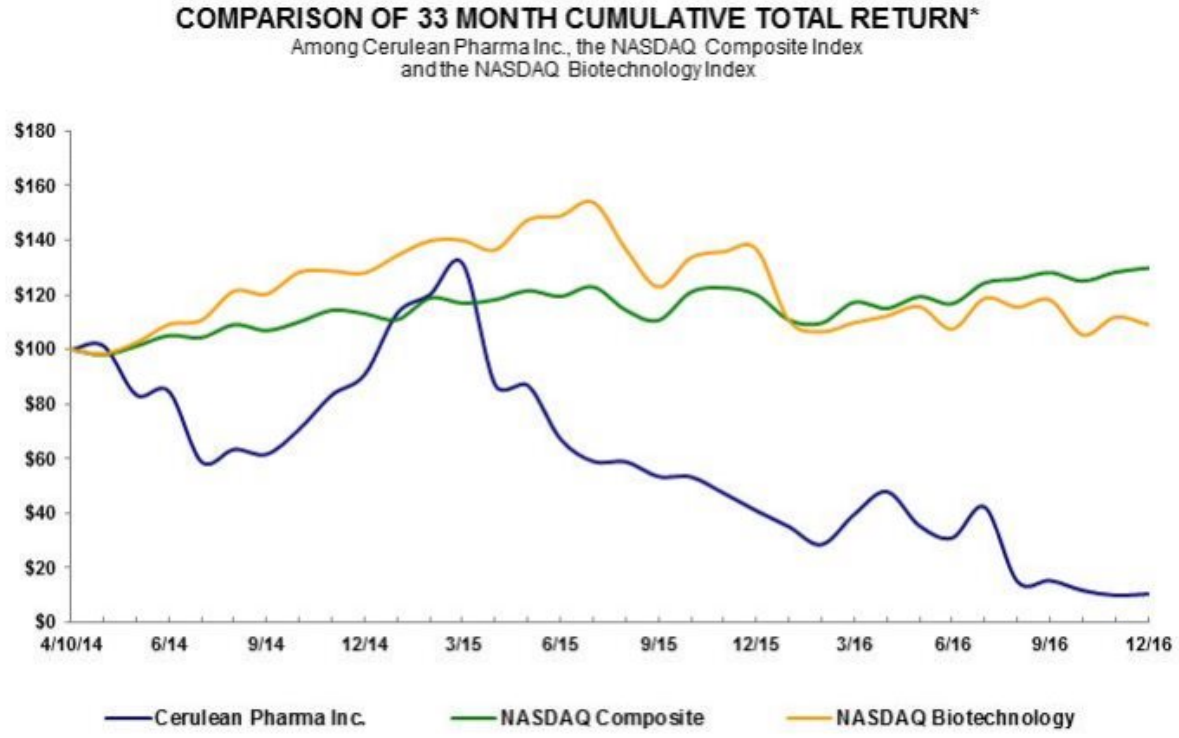
We completed the initial public offering of our common stock, or our IPO, pursuant to a Registration Statement on Form S-1 (File No. 333-194442), which was declared effective by the United States Securities and Exchange Commission, or SEC, on April 10, 2014. The net offering proceeds to us, after deducting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

As of December 31, 2016, we had used all of the net proceeds from our IPO, primarily to fund the clinical development of CRLX101, to fund research and development of CRLX301 and for working capital and other general corporate purposes. There was no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act.

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, or the 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 our company under the Securities Act of 1933, as amended, or the Exchange Act.

The following graph compares the cumulative total return to stockholders for our common stock for the period from April 10, 2014 through December 31, 2016 with The NASDAQ Composite Index and the NASDAQ Biotechnology index. The comparison assumes an investment of $100 is made on April 10, 2014 in our common stock 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. ***S elected 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, 2016, 2015, and 2014, and the consolidated balance sheet data at December 31, 2016 and 2015 from our audited consolidated financial statements included in this report on Form 10-K. The consolidated statement of operations data for the years ended December 31, 2013 and 2012, and consolidated balance sheet data as of December 31, 2014, 2013 and 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)	**2016**	**2015**	**2014**	**2013**	**2012**
Consolidated Statement of Operations Data:					
Revenue	$ 766	$ —	$ 80	$ 6	$ 625
Operating expenses:					
Research and development	27,565	25,948	11,772	9,700	15,807
General and administrative	10,355	11,224	8,587	6,166	6,393
Total operating expenses	37,920	37,172	20,359	15,866	22,200
Other income (expense):					
Interest income	86	10	9	2	2
Interest expense	(2,237)	(2,432)	(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	(2,151)	(2,422)	(3,063)	(1,283)	(526)
Net loss	(39,305)	(39,594)	(23,342)	(17,143)	(22,101)
Accretion of redeemable convertible preferred stock	—	—	—	—	(73)
Net loss attributable to common stockholders	$ (39,305)	$ (39,594)	$ (23,342)	$ (17,143)	$ (22,174)
Net loss per share attributable to common stockholders:					
Basic and diluted	$ (1.42)	$ (1.56)	$ (0.92)	$ (1.18)	$ (36.39)
Weighted-average common shares outstanding:					
Basic and diluted	27,710,403	25,431,332	25,431,332	14,548,516	609,344

	As of December 31,				
(in thousands)	**2016**	**2015**	**2014**	**2013**	**2012**
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 34,950	$ 75,908	$ 51,174	$ 5,488	$ 16,707
Working capital (deficit)	$ 19,851	$ 60,965	$ 44,775	$ (8,699)	$ 10,540
Total assets	$ 37,688	$ 78,225	$ 53,393	$ 6,827	$ 17,661
Long-term debt (including current portion)	$ 12,821	$ 20,324	$ 3,124	$ 6,258	$ 9,127
Redeemable convertible preferred stock	$ —	$ —	$ —	$ 81,525	$ 83,751
Common stock	$ 3	$ 3	$ 2	$ —	$ —
Additional paid in capital	$ 213,788	$ 210,115	$ 167,104	$ 4,140	$ 1,257
Accumulated deficit	$ (200,680)	$ (161,375)	$ (121,781)	$ (98,439)	$ (81,296)
Total stockholders' equity (deficit)	$ 13,111	$ 48,743	$ 45,325	$ (94,299)	$ (80,039)

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing elsewhere in this 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 an oncology-focused company applying our proprietary Dynamic Tumor Targeting™ Platform, or the 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.

In February 2017, we announced that our board of directors initiated a review of strategic alternatives that could result in changes to our business strategy and future operations. As part of this process, our board determined to review alternatives with the goal of maximizing stockholder value, including a potential sale of the company, a reverse merger, a business combination or a sale, license or other disposition of company assets.

On March 19, 2017, we entered into a stock purchase agreement, or the Stock Purchase Agreement, with Daré Bioscience, Inc., or Daré, and the holders of capital stock and securities convertible into capital stock of Daré named therein, or the Selling Stockholders, pursuant to which, among other things, the Selling Stockholders agreed to sell to us, and we agreed to purchase from the Selling Stockholders, all of the outstanding shares of capital stock, including those issuable upon conversion of convertible securities, of Daré. We refer to this transaction as the Daré Transaction. Immediately following the closing of the Daré Transaction, we expect that the Selling Stockholders will own between approximately 51% and 70% (depending on the net cash positions of us and Daré at closing) of the outstanding equity securities of Cerulean Pharma Inc.

Consummation of the Daré Transaction is subject to certain closing conditions, including, among others, (1) approval of the issuance of the shares of our common stock in the Daré Transaction by our stockholders in accordance with applicable NASDAQ Stock Ma rket, Inc., or NASDAQ, rules, which (assuming a quorum is present) require the affirmative vote of a majority of the shares of our common stock, present in person or represented by proxy and entitled to vote on the subject matter (excluding broker non-votes and abstentions), (2) the absence of any order, executive order, stay, decree, judgment or injunction or statute, rule or regulation that makes the consummation of the Daré Transaction illegal, or otherwise prohibits the consummation of the Daré Transact ion, and (3) the approval of the NASDAQ Initial Listing Application—For Companies Conducting a Business Combination that Results in a Change of Control with respect to the shares of our common stock to be issued in connection with the Daré Transaction. Eac h party's obligation to consummate the Daré Transaction is also subject to other specified customary conditions, including (1) the representations and warranties of the other party (with Daré and the Selling Stockholders being considered together for such purposes) being true and correct as of the date of the Stock Purchase Agreement and as of the closing date of the Daré Transaction, generally subject to an overall material adverse effect qualification, and (2) the performance in all material respects by t he other party (with Daré and the Selling Stockholders being considered together for such purposes) of its obligations under the Stock Purchase Agreement. The Stock Purchase Agreement contains certain termination rights for both us and Daré, and further provides that, upon termination of the Stock Purchase Agreement under specified circumstances, we may be required to pay Daré a termination fee of $0.3 million, or Daré may be required to pay us a termination fee of $0.45 million. There can be no assurances that the Daré Transaction will be consummated.

On March 19, 2017, we also entered into an asset purchase agreement, or the Novartis Asset Purchase Agreement, with Novartis Institutes for BioMedical Research, Inc., or Novartis. Under the Novartis Asset Pu rchase Agreement, we agreed to sell and assign to Novartis all of our right, title and interest in and to the patent rights, know-how and third-party license agreements relating to the Platform. We refer to this transaction as the Novartis Transaction. A t the closing of the Novartis Transaction, Novartis will be obligated to pay us a purchase price of $6.0 million.

We refer to the Daré Transaction , the Novartis Transaction and the BlueLink Asset Purchase Agreement as the 2017 Strategic Transactions.

Consummation of the Novartis Transaction is subject to us obtaining, pursuant to Delaware law, the approval of the holders of at least a majority of our common stock for the sale of substantially all of our assets in the Novartis Transaction. Each party's obligation to consummate the Novartis Transaction is also subject to other specified customary conditions, including (1) the representations and warranties of the other party being true and correct as of the closing date of the Novartis Transaction, generally subject in the case of

Novartis' representations and warranties to an overall materiality qualification, and (2) the performance in all material respects by the other party of its obligations under the Novartis Asset Purchase Agreement, including in our c ase by obtaining all necessary corporate and third-party consents. There can be no assurances that the Novartis Transaction will be consummated.

On March 19, 2017, we also entered into an Asset Purchase Agreement with BlueLink Pharmaceuticals, Inc., or BlueLink, a subsidiary of NewLink Genetics Corporation. We refer to this as the BlueLink Asset Purchase Agreement. Under the BlueLink Asset Purchase Agreement we sold and assigned to BlueLink all of our right, title and interest in and to our clinical product candidates CRLX101 and CRLX301, or the Products. We also transferred and assigned to BlueLink the accompanying intellectual property rights and know-how to the Products. On March 21, 2017, BlueLink paid the purchase price of $1.5 million. Also in connection with the BlueLink Asset Purchase Agreement, we and BlueLink entered into a license agreement in favor of BlueLink, pursuant to which we agreed to grant to BlueLink an exclusive, worldwide, perpetual, sublicensable right and license, under the Platform, to research, develop and commercialize the Products. Pursuant to the Novartis Asset Purchase Agreement, Novartis will assume this license agreement upon the closing of the Novartis Transaction.

On March 17, 2017, we entered into a payoff letter with Hercules Capital, Inc. (formerly known as Hercules Technology Growth Capital, Inc.), or Hercules, pursuant to which we agreed to pay off and thereby terminate our Loan and Security Agreement dated as of January 8, 2015, or the Hercules Loan Agreement, with Hercules as lender. Pursuant to the payoff letter, we paid, on March 20, 2017, a total of $12.4 million to Hercules, representing the principal, accrued and unpaid interest, fees, costs and expenses outstanding under the Hercules Loan Agreement in repayment of our outstanding obligations under the Hercules Loan Agreement. This payoff amount included a final end of term charge to Hercules in the amount of $1.4 million, representing 6.7% of the aggregate original principal amount advanced by Hercules. Upon the payment of the $12.4 million pursuant to the payoff letter, all outstanding indebtedness and obligations to Hercules under the Hercules Loan Agreement were deemed paid in full, and the Hercules Loan Agreement was terminated.

On March 20, 2017, we announced a restructuring including the elimination of approximately 58% of our workforce, to a total of eight full-time equivalent employees, under a plan expected to be completed during the second quarter of 2017.

The Platform is designed to create nanoparticle-drug conjugates, or NDCs, with the aim of providing safer and more effective therapies for patients living with cancer. NDCs consist of anti-cancer therapeutics, or payloads, covalently linked to a proprietary polymer. An important goal for all drugs is to maximize the net clinical benefit by increasing the desired therapeutic effect while reducing adverse effects. This is especially difficult with drugs used to treat cancer, where the goal is to destroy or inhibit growth of cancer cells without damaging healthy cells. We believe NDCs concentrate their anti-cancer payloads inside tumor cells while sparing normal tissue because they are small enough to pass through the leaky pores of new blood vessels in tumors as an entry portal into tumor tissue, but are too large to pass through the pores of healthy blood vessels. Once inside tumors, we believe NDCs are actively taken up into tumor cells where they slowly release their anti-cancer payloads, providing a durable inhibition of their targets.

Based on their properties and design, NDCs have the potential to enable synergistic combination therapies that can offer better tolerability and efficacy. We believe that better tolerability can be achieved through the preferential accumulation of the NDC in the tumor cells while better efficacy can be achieved by combining drugs that have different and complementary mechanisms of action. Cancer is a multi-faceted disease that is rarely adequately addressed by one therapy. Tumor cells are genetically diverse and can rapidly resist and ultimately overcome a single-agent therapy by modulating various adaptive pathways; however, if multiple drugs simultaneously shut down multiple adaptive pathways, there is a greater chance of achieving favorable disease responses for an extended period of time.

The Platform generated two clinical-stage NDCs. The first clinical candidate generated by the Platform, CRLX101, is an NDC with a camptothecin payload. Camptothecin is a potent topoisomerase 1, or topo 1, inhibitor that was too toxic to develop in the clinic; however, CRLX101 reduces the toxicities associated with this highly potent agent, while increasing the payload concentration in tumors. The second clinical candidate generated by the Platform, CRLX301, is an NDC with a docetaxel payload. Docetaxel is a commercially successful oncology drug that suffers from significant toxicities. We sold both clinical candidates to BlueLink on March 19, 2017.

In August 2016 we announced top-line results from our Phase 2, randomized, multi-center clinical trial of CRLX101 in combination with Avastin in the treatment of patients with advanced renal cell carcinoma, or RCC. We refer to this trial as the RCC Trial. The RCC Trial was conducted at 43 sites in the United States and South Korea, and enrolled 115 patients with RCC who progressed through two or three prior lines of therapy. Patients were randomized to receive CRLX101 in combination with Avastin or investigator's choice standard of care, or SOC, therapy. The primary endpoint was progression free survival, or PFS, in the clear cell population assessed by independent radiological review. Secondary endpoints included overall response rate, duration of response and overall survival. The study demonstrated no statistically significant difference in median PFS and objective response rate for the CRLX101 and Avastin combination compared to SOC. The CRLX101 and Avastin combination appeared to be safe and well-tolerated and the safety and tolerability profile of the combination was consistent with that observed in previous studies. We presented

the full data set from the RCC Trial at the Fifteenth International Kidney Cancer Sympos ium in November 2016. Based on these top-line results, we submitted a letter to the FDA voluntarily surrendering the Fast Track Designation in metastatic RCC we received in April 2015. We discontinued development of CRLX101 in this indication.

Following the announcement of the RCC Trial data we announced in August 2016 that our board of directors approved a plan to reduce the size of our workforce by approximately 48% to a total of 23 full-time equivalent employees. The workforce reduction, which was substantially completed in December 2016, was designed to reduce our operating expenses while we conducted a review of development options for CRLX101. As of December 31, 2016, we had 19 full-time employees.

In October 2016, we entered into a research collaboration agreement with Novartis. Under the collaboration agreement, we will create NDC candidates using the Platform and Novartis-selected active pharmaceutical ingredients, and Novartis will be responsible for the development and commercialization of NDC products resulting from the collaborative research efforts. The initial research term of the collaboration agreement is two years which may be extended for up to two additional one-year terms. We received a $5.0 million upfront payment under the collaboration agreement, and are entitled to receive additional research, development, regulatory and sales milestone payments, as well as royalties on net sales of any NDC product commercialized by Novartis. In addition, we are entitled to receive funding for up to five full-time employees to be engaged in activities under the collaboration during the research term. If the Novartis Transaction is consummated, this collaboration agreement will be superseded by the Novartis Asset Purchase Agreement.

To date, we have devoted substantially all of our resources to our drug discovery and development efforts, including conducting clinical trials of the Products (which we sold in March 2017 to BlueLink), protecting our intellectual property and the general and administrative support of our operations. We have generated no revenue from product sales and do not expect to generate any revenue from product sales for the next several years, if ever. Through December 31, 2016, we have funded our operations primarily through $84.2 million in proceeds from the sale of shares of our convertible preferred stock in private placements, net proceeds of $59.9 million from sales of shares of our common stock in our initial public offering, or IPO, net proceeds of $37.2 million from the sale of shares of our common stock in April 2015 in an underwritten public offering, $17.3 million in proceeds from our sale of convertible promissory notes, $10.0 million in proceeds from a loan and security agreement with Lighthouse Capital Partners VI, L.P., or Lighthouse Capital, and $21.0 million in proceeds from the Hercules Loan Agreement. We refer to our loan and security agreement with Lighthouse Capital as the Lighthouse Loan Agreement. In October 2016, we entered into a common stock purchase agreement with Aspire Capital Fund, LLC, or Aspire, for a $20.0 million firm commitment at-the-market equity facility, which we refer to as the ATM. In connection with entry into the ATM, Aspire made an initial $1.0 million investment and we have not made any other sales to date under the ATM.

We have never been profitable and have incurred significant operating losses since our incorporation. As of December 31, 2016, we had an accumulated deficit of $200.7 million. We incurred net losses of $39.3 million, $39.6 million, and $23.3 million for the years ended December 31, 2016, 2015 and 2014, respectively.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and from year to year. If we do not consummate the Daré Transaction and/or the Novartis Transaction, we will need to raise additional capital in the future to support our expenses and operating activities. If we are unable to obtain additional funding on a timely basis, we may be required to curtail or terminate research and development activities under our collaboration agreement with Novartis, or to scale back, suspend or terminate our business operations.

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 2016 we generated revenue from research and development payments under our collaboration agreement with Novartis. Prior to 2016, our only revenue was attributable to a government tax credit that we received in 2010 and payments in each of the years from 2011 through 2014 from four material transfer agreements and a research agreement.

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 product candidates. If we fail to complete the development of product candidates in a timely manner or to obtain regulatory approval for such product candidates, our ability to generate future revenue and our results of operations and financial position would be materially adversely affected.

Research and Development Expenses

Research and development expense reflected on our financial statements consists of costs incurred in connection with the discovery and development of the Platform and NDCs. These expenses consist primarily of:

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

We expense research and development costs as incurred.

Conducting a significant amount of research and development has been central to our business model for the periods covered by this Annual Report on Form 10-K. 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 expect our research and development expenses will decrease for 2017 compared to prior years.

We have used 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, 2016, 2015 and 2014 (in thousands):

	Years Ended December 31,		
	2016	2015	2014
CRLX101	$ 19,888	$ 19,026	$ 7,235
CRLX301	4,207	3,466	2,446
Dynamic Tumor Targeting Platform	2,267	2,103	1,212
Overhead	1,203	1,353	879
Total research and development expense	$ 27,565	$ 25,948	$ 11,772

The following summarizes the programs for which we have incurred the most significant research and development expense.

CRLX101 and CRLX301

CRLX101 was our lead product candidate until March 2017. There are two ongoing clinical trials of CRLX101 in this indication: (1) a Phase 1b/2 company-sponsored trial of CRLX101 in combination with weekly paclitaxel in patients with relapsed ovarian cancer in collaboration with GOG Foundation, Inc. (formerly known as the Gynecologic Oncology Group); and (2) a Phase 2 Investigator Sponsored Trial, or IST, exploring CRLX101 as monotherapy and in combination with Avastin in patients with relapsed ovarian cancer, conducted by Massachusetts General Hospital and affiliated Harvard University teaching hospitals.

Additional trials involving CRLX101 are also ongoing, including (1) a Phase 1/2 clinical trial sponsored by the National Cancer Institute, ev aluating the combination of CRLX101 and LYNPARZA™ (olaparib) in patients with advanced solid tumors, and (2) a Phase 1b company-sponsored trial exploring a dose-intensive schedule for CRLX101 in patients with solid tumors, which includes an arm exploring weekly CRLX101 in combination with a chemotherapy regimen known as FOLFOX in solid tumor patients.

CRLX301 was our second product candidate. CRLX301 is currently being evaluated in a Phase 1/2a trial in patients with advanced solid tumor malignancies in or der to establish the safety of the drug and the maximum tolerated dose for two dosing schedules.

In March 2017, we sold and assigned to BlueLink all of our right, title and interest in and to CRLX101 and CRLX301. As a result, we will not incur additional research and development expenses with respect to these programs in future periods.

The Platform

If the Novartis Transaction is not consummated, our board of directors decides to continue to operate the Platform, and if we are able to raise additional funds, we would expect that the expenses related to our NDCs and the development of the Platform would increase in 2017 as compared to 2016 as we would focus on research, development and strategic collaborations with new partners and we would need additional staffing to operate the Platform. We cannot accurately predict future research and development expenses for NDCs because such costs are dependent on a number of variables, including the success of potential future collaborations and preclinical studies of any such NDC. If the Novartis Transaction is consummated, we expect that we would not incur any significant expenses related to the Platform in future periods.

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

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

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

As a result of the uncertainties discussed above, we are unable to determine when, or to what extent, we will generate revenues from the commercialization and sale of any NDC either on our own or as part of a collaboration. We anticipate that, if the Novartis Transaction is not consummated, we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical data with respect to each NDC, our then-current financial condition, agreements with collaborators, and ongoing assessment of the NDCs' commercial potential. We will need to raise additional capital in the future in order to fund the development of any NDCs.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and related costs for personnel in our executive, finance, business development, 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 expect that our general and administrative expenses will decrease for 2017 as compared to 2016 as a result of our reduction in force and other cost control measures.

Interest Income

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

Interest Expense

Interest expense consists primarily of interest, amortization of debt discount and amortization of deferred financing costs associated with the Hercules Loan Agreement. Interest expense also includes the write off of debt discount and deferred financing costs associated with the repayment in 2015 of the debt incurred under the Lighthouse Loan Agreement. In 2014, interest expense consisted primarily of interest, amortization of debt discount and amortization of deferred financing costs associated with the Lighthouse Loan Agreement and interest expense on our convertible notes. We expect that our interest expense will decrease for 2017 as compared to 2016 as a result of our repayment in full of all amounts outstanding under, and termination of, the Hercules Loan Agreement in March 2017.

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.

Revenue Recognition

Prior to the 2017 Strategic Transactions, our business strategy included entering into collaborative license and development agreements for the development and commercialization of product candidates utilizing the Platform. The terms of these arrangements typically included multiple deliverables by us (such as granting of license rights, providing research and development services, manufacturing of clinical materials and participating on joint research committees) in exchange for consideration to us of some combination of one or more of non-refundable license fees, funding of research and development activities, payments based upon achievement of clinical development, regulatory and sales milestones and/or royalties in the form of a designated percentage of product sales or participation in profits.

Revenue arrangements with multiple deliverables are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the collaborative partner and based on the selling price of the deliverables. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method using management's best estimate of the standalone selling price of deliverables when vendor-specific objective evidence or third-party evidence of selling price is not available. Allocated consideration is recognized as revenue upon application of the appropriate revenue recognition principles to each unit.

The assessment of multiple deliverable arrangements requires judgment in order to determine the appropriate units of accounting, the estimated selling price of each unit of accounting, and the points in time that, or periods over which, revenue should be recognized.

For the year ended December 31, 2016, we reported $766,000 of collaborative research and development revenue, which includes $259,000 of revenue for funding from our collaborative partner to be engaged in activities under the collaboration during the research term. We recorded no revenue from collaborative license and development agreements during the prior year. Revenue is recognized when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed and determinable and collection is reasonably assured.

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* . 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.

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.

Results of Operations

Comparison of the Years Ended December 31, 2016 and 2015

The following table summarizes our consolidated results of operations for the years ended December 31, 2016 and 2015, together with the changes in those items in dollars and as a percentage (in thousands, except percentages):

	Years Ended December 31,		Change	
	2016	2015	Dollar	%
Revenue	$ 766	$ —	$ 766	—
Operating expenses:				
Research and development	27,565	25,948	1,617	6%
General and administrative	10,355	11,224	(869)	(8)%
Loss from operations	(37,154)	(37,172)	18	0%
Other expense, net	(2,151)	(2,422)	271	(11)%
Net loss	$ (39,305)	$ (39,594)	$ 289	-1%

Revenue. Revenue for the year ended December 31, 2016 was $0.8 million from the recognition of research and development payments under the Novartis collaboration agreement including $0.5 million of upfront fees, which is being recognized as revenue on a straight-line basis over the initial research term, as well as $0.3 million of fees for direct research services. There was no revenue for the year ended December 31, 2015.

Research and development. Research and development expense for the year ended December 31, 2016, was $27.6 million compared to $25.9 million for the year ended December 31, 2015, an increase of $1.6 million, or 6%. The increase was attributable to an increase in co st s associated with each of our former clinical programs. The following table summarizes our research and development expense by program for the years ended December 31, 2016 and 2015, together with the change in spending by program in dollars and as a perc entage (in thousands, except percentages):

	Years Ended December 31,		Change	
	2016	2015	Dollar	%
CRLX101	$ 19,888	$ 19,026	$ 862	5%
CRLX301	4,207	3,466	741	21%
Dynamic Tumor Targeting Platform	2,267	2,103	164	8%
Overhead	1,203	1,353	(150)	(11)%
Total research and development expense	$ 27,565	$ 25,948	$ 1,617	6%

For the year ended December 31, 2016, CRLX101 program expenses increased by $0.9 million, or 5%, to $19.9 million compared to $19.0 million for the year ended December 31, 2015. The increase in CRLX101 program expenses was primarily attributable to chemistry, manufacturing, and controls, or CMC, for which costs increased $1.4 million, reflecting increased production and activity to support then-current and future clinical development of CRLX101. Salary and benefits expenses also increased $0.8 million, reflecting increased headcount to support the CRLX101 program and the CRLX101 clinical trials. These increases were partially offset by a decrease of $1.3 million in clinical trial expenses, reflecting a decrease in CRO fees, investigator fees and costs associated with clinical sites and laboratories.

For the year ended December 31, 2016, CRLX301 program expenses increased $0.7 million, or 21%, to $4.2 million compared to $3.5 million for the year ended December 31, 2015. The increase in CRLX301 program expense was attributable to an increase of $0.5 million in clinical trial expenses, consisting primarily of increases in CRO and laboratory costs and an increase of $0.2 million in salary and benefits expenses reflecting increased headcount to support the CRLX301 program and the CRLX301 clinical trials.

Expenses associated with the Platform were $2.3 million for the year ended December 31, 2016, an increase of $0.2 million, or 8%, compared to $2.1 million for the year ended December 31, 2015. The increase was primarily due to increased salary and benefits expenses combined with increases in consulting and external lab costs. Overhead costs decreased $0.2 million, or 11%, to $1.2 million for the year ended December 31, 2016 compared to $1.4 million for the year ended December 31, 2015. The decrease was primarily attributable to a decrease in facility costs.

General and administrative. General and administrative expense for the year ended December 31, 2016, was $10.3 million compared to $11.2 million for the year ended December 31, 2015, a decrease of $0.9 million, or 8%. The decrease in general and administrative costs was primarily due to reduced headcount and cost control measures taken in the second half of 2016.

Other expense, net. Other expense, net, was $2.2 million for the year ended December 31, 2016, a decrease of $0.2 million, or 11%, compared to $2.4 million for the year ended December 31, 2015. For the years ended December 31, 2016 and 2015, other expense, net, was primarily interest expense associated with the Hercules Loan Agreement, including $0.4 million and $0.5 million in each year, respectively, for the amortization of debt discount and deferred financing costs. For the year ended December 31, 2015, interest expense included $0.2 million for the write off of debt discount and deferred financing costs associated with the repayment of the Lighthouse Loan Agreement.

Comparison of the Years Ended December 31, 2015 and 2014

The following table summarizes our consolidated results of operations for the years ended December 31, 2015 and 2014, together with the changes in those items in dollars and as a percentage (in thousands, except percentages):

	Years Ended December 31,		Change	
	2015	2014	Dollar	%
Revenue	$ -	$ 80	$ (80)	(100)%
Operating expenses:				
Research and development	25,948	11,772	14,176	120%
General and administrative	11,224	8,587	2,637	31%
Loss from operations	(37,172)	(20,279)	(16,893)	83%
Other expense, net	(2,422)	(3,063)	641	(21)%
Net loss	$ (39,594)	$ (23,342)	$ (16,252)	70%

Revenue. There was no revenue recorded for the year ended December 31, 2015. For the year ended December 31, 2014, we recorded revenue of $80,000 from payments we received under two material transfer agreements. Pursuant to the agreements, we received payments in exchange for providin g research services utilizing our proprietary technology. Work under the agreements terminated in 2014.

Research and development. Research and development expense for the year ended December 31, 2015, was $25.9 million compared to $11.8 million for the year ended December 31, 2014, an increase of $14.1 million, or 120%. The increase was primarily attributable to an increase in costs associated with the CRLX101 program. The following table summarizes our research and development expense by program for the years ended December 31, 2015 and 2014, together with the change in spending by program in dollars and as a percentage (in thousands, except percentages):

	Years Ended December 31,		Change	
	2015	2014	Dollar	%
CRLX101	$ 19,026	$ 7,235	$ 11,791	163%
CRLX301	3,466	2,446	1,020	42%
Dynamic Tumor Targeting Platform	2,103	1,212	891	74%
Overhead	1,353	879	474	54%
Total research and development expense	$ 25,948	$ 11,772	$ 14,176	120%

For the year ended December 31, 2015, CRLX101 program expenses increased by $11.8 million, or 163%, to $19.0 million compared to $7.2 million for the year ended December 31, 2014. The increase in CRLX101 program expense was primarily attributable to costs associated with our RCC Trial, which was initiated in mid-2014. Additional CRLX101 costs include costs associated with ISTs in addition to costs associated with clinical trials initiated in 2015 including our Phase 1b single-arm, company-sponsored trial of CRLX101 in combination with weekly paclitaxel in patients with relapsed ovarian cancer and our Phase 1 trial exploring a dose-intensive schedule for CRLX101 in patients with advanced solid tumor malignancies . Clinical trial expenses increased $6.5 million reflecting an increase in CRO fees, investigator fees and costs associated with clinical sites and laboratories. Salary and benefits expenses increased $2.0 million and consulting costs increased $0.8 million compared to the prior year to support the CRLX101 development program and the clinical trials. Chemistry, manufacturing and controls costs increased $2.2 million compared to the prior year reflecting increased activity to support clinical development of CRLX101.

For the year ended December 31, 2015, CRLX301 program expenses increased $1.0 million, or 42%, to $3.4 million compared to $2.4 million for the year ended December 31, 2014. The increase in CRLX301 program expenses was primarily due to costs associated with the Phase 1/2a clinical trial that we initiated in December 2014. CRLX301 clinical trial expenses increased by $0.5 million for the year ended December 31, 2015, compared to the prior year primarily due to CRO fees, costs associated with clinical sites and laboratory costs. Salary and benefits expenses increased $0.5 million and consulting costs increased $0.2 million to support the CRLX301 program development and the clinical trials. The increase in costs associated with the CRLX301 program were partially offset by a milestone fee of $0.3 million paid to Calando upon initiation of the CRLX301 clinical trial in 2014 compared to no milestone fee in 2015.

Expenses associated with our Dynamic Tumor Targeting Platform were $2.1 million for the year ended December 31, 2015, an increase of $0.9 million, or 74%, compared to $1.2 million for the year ended December 31, 2014. The increase is primarily due to increased headcount and lab costs in new discovery research. Overhead costs increased $0.5 million, or 54%, to $1.4 million compared to $0.9 million for the year ended December 31, 2014. The increase was primarily attributable to increases in facility and depreciation costs of $0.2 million, recruiting and employee costs of $0.2 million and other costs of $0.1 million not allocated to programs.

General and administrative. General and administrative expense for the year ended December 31, 2015, was $11.2 million compared to $8.6 million for the year ended December 31, 2014, an increase of $2.6 million, or 31%. The increase in general and administrative costs was attributable to the growth in our corporate infrastructure to support our increased size as well as requirements resulting from our being a public company. Salaries and benefits, including stock-based compensation, increased $2.1 million for the year ended December 31, 2015, compared to the prior year, reflecting increases in finance and accounting, legal and corporate communications staffing. Other general and administrative expenses including professional services and consulting, facility and office expenses, dues and subscriptions, conference and travel expenses increased $0.2 million for the year ended December 31, 2015, compared to the prior year due to our overall growth.

Other expense, net. Other expense, net, for the year ended December 31, 2015, was $2.4 million compared to $3.1 million for the year ended December 31, 2014, a decrease of $0.7 million, or 21%. The decrease in other expense, net, was primarily due to a $2.5 million loss on the conversion of the 2014 Convertible Notes, which was recorded in April 2014. Interest expense was $2.4 million and $1.1 million for the years ended December 31, 2015 and 2014, respectively, an increase of $1.3 million, or 121%. For the

year ended December 31, 2015, interest expense included $2.1 million associated with the Hercules Loan Agreement, including $0.5 million for the amortization of debt discount and deferred financing costs, and $0.2 million for the write off of debt discount and deferred financing costs associated with the repayment of the Lighthouse Loan Agreement. Interest expense for the year ended December 31, 2014, included $0.3 million of interest on our convertible notes and $0.6 million of interest and $0.2 million for amortization of debt discount and deferred financing cost s associated with the Lighthouse Loan Agreement. Other expense, net, for the year ended December 31, 2014, included a $0.5 million adjustment to the fair value of our outstanding preferred stock warrant liability which was recorded as other income.

Liquidity and Capital Resources

From our incorporation through December 31, 2016, we raised an aggregate of $236.6 million to fund our operations, of which $84.2 million was from the sale of preferred stock in private placements, $59.9 million was from the IPO, $37.2 million was from our follow-on offering in April 2015, $17.3 million was from the sale of convertible promissory notes, $31.0 million was from borrowings under loan and security agreements, $1.0 million was from the private placement of our common stock to Hercules, $1.0 million was from the initial purchase by Aspire under the ATM and $5.0 million was from the upfront payment under the collaboration agreement with Novartis. As of December 31, 2016, we had cash and cash equivalents of $35.0 million.

Indebtedness

Hercules Loan Agreement. On January 8, 2015, we entered into the Hercules Loan Agreement and borrowed $15.0 million from Hercules. We used a portion of those proceeds to repay our outstanding indebtedness under the Lighthouse Loan Agreement. The Hercules Loan Agreement provided for up to three separate tranches of borrowings, the first of which was funded in the amount of $15.0 million on January 8, 2015. On November 24, 2015, we drew a second tranche in the amount of $6.0 million.

Our indebtedness under the Hercules Loan Agreement was scheduled to mature on July 1, 2018. Each advance under the Hercules Loan Agreement accrued interest at a floating per annum rate equal to the greater of (i) 7.30% or (ii) the sum of 7.30% plus the prime rate minus 5.75%. The Hercules Loan Agreement provided for interest-only payments on a monthly basis until December 31, 2015. Thereafter, payments were 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. At the end of the loan term (whether at maturity, by prepayment in full or otherwise), we were required to pay a final end-of-term charge to Hercules in the amount of 6.7% of the aggregate original principal amount advanced by Hercules.

In March 2017 we paid $12.4 million to Hercules, representing the principal, accrued and unpaid interest, fees, costs and expenses outstanding under the Hercules Loan Agreement in repayment in full of our outstanding obligations under the Hercules Loan Agreement and the Hercules Loan Agreement was terminated. There were no prepayment charges associated with the early repayment of the loan.

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

Aspire ATM . In connection with entry into the ATM, Aspire made an initial $1.0 million investment and we have not made any other sales to date under the ATM. While we may be able to make additional sales to Aspire under the ATM, we have historically not done so because we believed that the prices at which we would have been able to sell our common stock would have resulted in significant dilution.

Plan of Operations and Future Funding Requirements

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

As of December 31, 2016, we had cash and cash equivalents of $35.0 million. We have no other sources of significant liquidity in place as of December 31, 2016. We expect that our existing cash and cash equivalents will fund our operations into the second half of 2017 based on our 2017 operating plan. We have undertaken a strategic review of potential financing alternatives such as the sale of the company, a merger, a business combination, a strategic investment into the company, or a sale, license or disposition of our assets. Our recurring use of cash to fund operations in combination with the rate of expenditures with no known probable source of

capital raises substantial doubt about our ability to continue as a going concern. If we are unable to obtain additional funding on a timely basis, we may be required to curtail or terminate research and development activities under our collaboration agreement with Novartis, or to scale back, suspend or terminate our business operations.

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

- whether and when we are able to consummate the Daré Transaction and/or the Novartis Transaction;
- the number and development requirements of the NDCs we or any collaborators pursue;
- the scope, progress, timing, results and costs of researching and developing NDCs, and conducting preclinical studies and clinical trials;
- the costs, timing and outcome of regulatory review of NDCs in the United States and abroad;
- the cost and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any NDCs for which we or a collaborator receive marketing approval;
- the revenue, if any, received from commercial sales of any NDCs for which we or a collaborator 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 NDCs and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our NDCs, if approved, may not achieve commercial success. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and revenue from collaboration arrangements. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or 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 any 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.

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,		
	2016	2015	2014
Net cash used in operating activities	$ (33,536)	$ (31,915)	$ (19,061)
Net cash used in investing activities	(418)	(484)	(185)
Net cash provided by financing activities	(7,004)	57,133	64,932
Net increase (decrease) in cash and cash equivalents	$ (40,958)	$ 24,734	$ 45,686

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.

During the year ended December 31, 2016, cash used in operating activities consisted of our net loss of $ 39.3 million and net cash used in changes in our operating assets and liabilities of $ 2.3 million, partially offset by deferred revenue of $4.5 million and net non-cash charges of $ 3. 6 million. Our net non-cash charges during the period consisted primarily of stock-based compensation expense. Cash used in changes in our operating assets and liabilities consisted primarily of a decrease in accounts payable and accrued expenses of $ 1.9 million, and an increase in accounts receivable, prepaid expenses and other current assets of $ 0.4 million.

During the year ended December 31, 2015, cash used in operating activities consisted of our net loss of $39.6 million partially offset by net non-cash charges of $3.3 million and net cash provided by changes in our operating assets and liabilities of $4.4 million. Our net non-cash charges during the period consisted primarily of stock-based compensation expense of $2.4 million and amortization of debt discount and deferred financing costs of $0.7 million. Cash provided by changes in our operating assets and liabilities consisted primarily of an increase in accounts payable and accrued expenses of $4.1 million, and a decrease in accounts receivable, prepaid expenses and other current assets of $0.3 million.

During the year ended December 31, 2014, cash used in operating activities consisted of our net loss of $23.3 million partially offset by net non-cash charges of $3.2 million and net cash provided by changes in our operating assets and liabilities of $1.1 million. Our net non-cash charges during the period consisted primarily of a charge for a loss on extinguishment of debt of $2.5 million and stock-based compensation expense of $0.9 partially offset by change in carry value of preferred stock warrant liability of $0.5 million. Cash provided by changes in our operating assets and liabilities consisted primarily of an increase in accounts payable and accrued expenses of $1.8 million, partially offset by an increase in accounts receivable, prepaid expenses and other current assets of $0.7 million.

Net Cash Used in Investing Activities

During the year ended December 31, 2016, net cash used in investing activities was primarily attributable to purchases of property and equipment of $0.5 million partially offset by cash proceeds of $0.1 million from a decrease in restricted cash used to collateralize a stand-by letter of credit issued as a security deposit on our former facility lease.

During the year ended December 31, 2015, net cash used in investing activities was primarily attributable to purchases of property and equipment of $0.3 million combined with an increase in restricted cash of $0.2 million to collateralize a stand-by letter of credit issued as a security deposit on our new facility lease.

During the year ended December 31, 2014, net cash used in investing activities was primarily attributable to purchases of property and equipment of $0.2 million.

Net Cash Provided by Financing Activities

During the year ended December 31, 2016, net cash used in financing activities was primarily attributable to principal payments of $7.9 million under the Hercules Loan Agreement partially offset by proceeds from the sale of common stock to Aspire of $0.8 million, net of offering costs, and the sale of common stock under our employee stock purchase plan of $0.1 million.

During the year ended December 31, 2015, net cash provided by financing activities was primarily due to net proceeds of $37.2 million from our follow-on offering in April 2015, proceeds of $21.0 million from our borrowings under the Hercules Loan Agreement, proceeds of $1.0 million from the sale of our common stock in a private placement to Hercules and proceeds of $1.6 million from the exercise of stock options. Net cash provided by financing activities was reduced by $3.3 million to repay in full amounts due under the Lighthouse Loan Agreement and cash paid for debt issuance costs of $0.4 million.

During the year ended December 31, 2014, net cash provided by financing activities was primarily due to net proceeds of $59.9 million from our IPO and proceeds of $8.5 million from the sale of convertible promissory notes. Net cash provided by financing activities was reduced by payments of $3.3 million under the Lighthouse Loan Agreement and cash paid for debt issuance costs of $0.2 million.

Contractual Obligations and Contingent Liabilities

The following summarizes our significant contractual obligations as of December 31, 2016 (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)	$ 2,494	$ 738	$ 1,616	$ 140	—
Debt Obligations (2)	$ 15,194	$ 9,215	$ 5,979	—	—

(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.

(2) Consists of payment obligations for principal and interest to Hercules under the Hercules Loan Agreement. As of December 31, 2016, we had $13.1 million in outstanding borrowings under the debt facility, bearing interest at 7.3% with a one-time final payment of 6.7% of the original principal amount of $21.0 million due on July 1, 2018. In March 2017, we paid $12.4 million to Hercules, representing the principal, accrued and unpaid interest, fees, costs and expenses outstanding under the Hercules Loan Agreement in repayment in full of our outstanding obligations under the Hercules Loan Agreement and the Hercules Loan Agreement was terminated.

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 will be borne by BlueLink, with respect to CRLX101 and CRLX301, and/or by Novartis, if the Novartis Transaction is consummated and include the following:

- Under the CRLX101 Agreement, Calando could receive: (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, based on sales of CRLX101 and (3) a percentage, ranging from the low- to mid-double digits, of any licensing or sublicensing income received from the license or sublicense of CRLX101.
- Under the Platform Agreement, we paid to Calando in January 2015 a $0.3 million clinical development milestone following the initiation of our Phase 1/2a clinical trial of CRLX301 in December 2014. In addition, under the Platform Agreement, Calando could receive: (1) additional milestone payments in an aggregate amount of up to approximately $18.0 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, based on sales of CRLX301 and (3) a percentage, in the low-double digits, of any licensing or sublicensing income received from the license or sublicense of CRLX301.

The contractual obligations table does not include potential payments that may be required 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.

In addition, the contractual obligations table does not include certain amounts that are conditionally owed to certain executives. On March 19, 2017, we entered into retention agreements with certain executive officers. These retention agreements supersede the provisions of such executive officers' employment agreements and retention letters with us providing for post-separation benefits, and provide for certain lump sum payments ranging from 6 to 18 months of salary, plus health and dental insurance coverage, while also providing the covered executives with a cash bonus upon completion of a change in control. Under the terms of the retention agreements, we may be required to pay up to approximately $1.8 million.

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 November 2016, the Financial Accounting Standards Board, or the FASB issued Accounting Standards Update 2016-18, "Statement of Cash Flows - Restricted Cash (Topic 230)". This new standard requires companies to include amounts generally described as restricted cash and restricted cash equivalents in cash and cash equivalents when reconciling beginning-of-period and

end-of-period total amounts shown on the statement of cash flows. This guidance is effective for annual and interim reporting periods beginning after December 15, 2017, and required retrospective application. We are currently evaluating the effect this standard will have on our consolidated financial statements and related disclosures.

In August 2016, the FASB issued Accounting Standards Update 2016-15, "Statement of Cash Flows (Topic 230)", or ASU 2016-15. ASU 2016-15 provides guidance to clarify how cash payments for debt prepayment or debt extinguishment costs are to be classified in the statement of cash flows. The standard is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years and requires retrospective application. We are currently evaluating the effect this standard will have on our consolidated financial statements and related disclosures.

In March 2016, the FASB issued Accounting Standards Update 2016-09, "Compensation – Stock Compensation (Topic 718)", or ASU 2016-09. ASU 2016-09 is intended to simplify various aspects of how share-based payments are accounted for and presented in financial statements. The standard is effective prospectively for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2016, with early adoption permitted. For amendments that are to be applied on a modified retrospective basis, a cumulative-effect adjustment will be calculated on the first day of the fiscal year of adoption, which will be recorded in retained earnings. We have early adopted ASU 2016-09 for our quarter ended December 31, 2016. As a result of our adoption of ASU 2016-09, we will track option deductions in our net operating loss deferred tax asset on a modified retrospective basis, and have included the option deductions in the December 31, 2016 deferred tax assets. In addition, our policy has been to estimate forfeitures as of the grant date. We will continue to maintain the policy to estimate forfeiture as of the grant date in the future. The gross deferred tax asset and valuation allowance as of December 31, 2016, increased $163,000 as a result of the cumulative effect of adoption of ASU 2016-09. The adoption of ASU 2016-09 did not have a material impact on our financial statements for the year ended and as of December 31, 2016.

In February 2016, the FASB issued Accounting Standards Update 2016-02, "Leases (Topic 842)", or ASU 2016-02, which provides new accounting guidance on leases. ASU 2016-02 requires lessees to recognize leases on their balance sheets, and leaves lessor accounting largely unchanged. The amendments in ASU 2016-02 are effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early application is permitted for all entities. ASU 2016-02 requires a modified retrospective approach for all leases existing at, or entered into after, the date of initial application, with an option to elect to use certain transition relief. We are currently evaluating the impact of this new standard on our consolidated financial statements and related disclosures.

In August 2014, the FASB issued Accounting Standards Update 2014-15, "Presentation of Financial Statements – Going Concern (Subtopic 205-40): Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern", or ASU 2014-15. ASU 2014-15 requires management to evaluate, at each annual and interim reporting period, whether there are conditions or events that raise substantial doubt about the entity's ability to continue as a going concern and provide related disclosures. ASU 2014-15 is effective for annual and interim reporting periods beginning January 1, 2017 and is not expected to have a material impact on our consolidated financial statements.

In May 2014, the FASB issued Accounting Standards Update 2014-09 (ASC 606), "Revenue from Contracts with Customers", or ASU 2015-09, which affects any entity that either enters into contracts with customers to transfer goods and services or enters into contracts for the transfer of nonfinancial assets. In August 2015, the FASB issued Accounting Standards Update 2015-14, "Revenue from Contracts with Customers" which defers the effective date of ASU 2014-09 for all entities by one year. ASU 2014-09, which has been codified with the Accounting Standards Codification as Topic 606, is now effective for public companies for annual reporting periods beginning after December 15, 2017, including interim periods within those reporting periods. ASC 606 outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. In addition, ASC 606 provides guidance on accounting for certain revenue-related costs including, but not limited to, when to capitalize costs associated with obtaining and fulfilling a contract. ASC 606 provides companies with two implementation methods. Companies can choose to apply the standard retrospectively to each prior reporting period presented (full retrospective application) or retrospectively with the cumulative effect of initially applying the standard as an adjustment to the opening balance of retained earnings of the annual reporting period that includes the date of initial application (modified retrospective application). Since ASU 2014-09 was issued, several additional Accounting Standards Updates have been issued and incorporated within ASC 606 to clarify various elements of the guidance. We plan to adopt this guidance on January 1, 2018. We have not yet determined whether we will utilize the full retrospective or the modified retrospective adoption method and continue to evaluate the impact that adoption will have on our consolidated financial statements.

I tem 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of December 31, 2016, we had cash and cash equivalents, including restricted cash, of $35.0 million, consisting primarily of investments in money market funds and certificates of deposit. Our

primary exposure to mar ket 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 r isk 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.

I tem 8. Financial Statements and Supplementary Data

CERULEAN PHARMA INC.

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R eport of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of
Cerulean Pharma Inc.
Waltham, Massachusetts

We have audited the accompanying consolidated balance sheets of Cerulean Pharma Inc. and subsidiary (the "Company") as of December 31, 2016 and 2015, 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, 2016. 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, 2016 and 2015, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2016, in conformity with accounting principles generally accepted in the United States of America.

The accompanying financial statements for the year ended December 31, 2016 have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company's recurring use of cash to fund operations in combination with the rate of expenditures with no known probable source of capital raises substantial doubt about its ability to continue as a going concern. Management's plans concerning these matters are also discussed in Note 1 to the financial statements. The accompanying financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 31, 2017

CERULEAN PHARMA INC.

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

	December 31,	
	2016	2015
ASSETS		
Current assets:		
Cash and cash equivalents	$ 34,950	$ 75,908
Accounts receivable, prepaid expenses, and other current assets	1,840	1,394
Total current assets	36,790	77,302
Property and equipment, net	668	576
Other assets	230	347
Total	$ 37,688	$ 78,225
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Current portion of loan payable	$ 8,382	$ 7,652
Accounts payable	1,446	2,226
Accrued expenses	4,611	6,459
Current portion of deferred revenue	2,500	—
Total current liabilities	16,939	16,337
Long-term liabilities:		
Loan payable, net of current portion	4,439	12,672
Deferred revenue	1,993	—
Other long-term liabilities	1,206	473
Total long-term liabilities	7,638	13,145
Commitments (Note 11)		
Stockholders' equity:		
Preferred stock $0.01 par value; 5,000,000 shares authorized, no shares issued or outstanding	—	—
Common stock, $0.0001 par value; 120,000,000 shares authorized, 28,937,185 and 27,346,780 shares issued and outstanding at December 31, 2016 and 2015, respectively	3	3
Additional paid-in capital	213,788	210,115
Accumulated deficit	(200,680)	(161,375)
Total stockholders' equity	13,111	48,743
Total	$ 37,688	$ 78,225

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,		
	2016	2015	2014
Revenue	$ 766	$ —	$ 80
Operating expenses:			
Research and development	27,565	25,948	11,772
General and administrative	10,355	11,224	8,587
Total operating expenses	37,920	37,172	20,359
Other income (expense):			
Interest income	86	10	9
Interest expense	(2,237)	(2,432)	(1,083)
Loss on extinguishment of debt	—	—	(2,493)
Decrease in value of preferred stock warrant liability	—	—	504
Total other income (expense), net	(2,151)	(2,422)	(3,063)
Net loss attributable to common stockholders	$ (39,305)	$ (39,594)	$ (23,342)
Net loss per share attributable to common stockholders:			
Basic and diluted	$ (1.42)	$ (1.56)	$ (1.60)
Weighted-average common shares outstanding:			
Basic and diluted	27,710,403	25,431,332	14,548,516

See notes to consolidated financial statements.

CERULEAN PHARMA INC.

CONSOLIDATED STATEMENT OF REDEEMABLE CONVERTIBLE 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 — January 1, 2014	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
Exercise of stock options			370,230		1,628		1,628
Stock-based compensation					2,375		2,375
Issuance of common stock from public offering, net of underwriting fees and issuance costs of $3,111			6,716,000	1	37,184		37,185
Issuance of common stock from private placement			135,501		1,000		1,000
Issuance of warrants in connection with term loan facility			—		824		824
Net loss						(39,594)	(39,594)
BALANCE — December 31, 2015	—	—	27,346,780	3	210,115	(161,375)	48,743
Issuance of common stock from employee stock purchase plan			37,712		78		78
Issuance of common stock for services			52,693		54		54
Stock-based compensation					2,755		2,755
Issuance of common stock from common stock purchase agreement, net of issuance costs of $214			1,500,000		786		786
Net loss						(39,305)	(39,305)
BALANCE — December 31, 2016	—	$ —	$ 28,937,185	$ 3	$ 213,788	$ (200,680)	$ 13,111

See notes to consolidated financial statements.

CERULEAN PHARMA INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS (In thousands)

	Years Ended December 31,		
	2016	2015	2014
Cash flows from operating activities:			
Net loss	$ (39,305)	$ (39,594)	$ (23,342)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	2,755	2,375	885
Noncash rent expense	153	(41)	29
Change in carrying value of preferred stock warrant liability	—	—	(504)
Depreciation and amortization	261	192	126
(Gain) loss on disposal of property and equipment	4	(6)	(28)
Loss on extinguishment of debt	—	—	2,493
Amortization of debt discount and deferred financing costs	420	739	215
Deferred revenue	5,000	—	—
Amortization of deferred revenue	(507)	—	—
Changes in operating assets and liabilities:			
Accounts receivable, prepaid expenses and other current assets	(446)	342	(695)
Accounts payable	(603)	795	341
Accrued expenses	(1,268)	3,283	1,419
Net cash used in operating activities	(33,536)	(31,915)	(19,061)
Cash flows from investing activities:			
Purchases of property and equipment	(535)	(277)	(225)
Proceeds from sale of property and equipment	—	23	40
Increase (decrease) in restricted cash	117	(230)	—
Net cash used in investing activities	(418)	(484)	(185)
Cash flows from financing activities:			
Proceeds from sale of common stock	918	2,628	140
Proceeds from public stock offering, net	—	37,185	59,862
Proceeds from loan payable	—	21,000	—
Proceeds from issuance of convertible promissory notes	—	-	8,500
Payments on loan payable	(7,922)	(3,321)	(3,348)
Cash paid for debt issuance costs	—	(359)	(222)
Net cash (used in) provided by financing activities	(7,004)	57,133	64,932
Net increase (decrease) in cash and cash equivalents	(40,958)	24,734	45,686
Cash and cash equivalents — Beginning of year	75,908	51,174	5,488
Cash and cash equivalents — End of year	$ 34,950	$ 75,908	$ 51,174
Supplemental disclosures of noncash investing and financing activities:			
Purchase of property and equipment in accounts payable	$ —	$ 177	$ —
Conversion of redeemable convertible preferred stock into common stock	$ —	$ —	$ 81,526
Conversion of convertible notes and accrued interest into common stock, net	$ —	$ —	$ 20,129
Reclassification of warrants to additional paid-in capital	$ —	$ —	$ 424
Warrants issued with term loan facility	$ —	$ 824	$ —
Supplemental cash flow information — Interest paid	$ 1,293	$ 1,000	$ 400

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 Waltham, 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.

The Company's operations have consisted primarily of raising capital, product research and development, and initial market development.

The Company has not generated any revenue related to its primary business purpose to date and is subject to a number of risks common to 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 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 $200.7 million at December 31, 2016. The Company has financed its operations primarily through private placements of its preferred stock, proceeds from borrowings, an initial public offering completed in 2014 and a follow-on offering completed in 2015. In October 2016 the Company entered into a collaboration with Novartis Institutes for BioMedical Research, Inc. ("Novartis") to develop nanoparticle-drug conjugates combining the Company's proprietary Dynamic Tumor Targeting technology with Novartis' proprietary compounds. Under this collaboration the Company received important funding to support its research program. The Company has not completed development of any product candidate and has devoted substantially all of its financial resources and efforts to research and development, including preclinical and clinical development. Accordingly, the Company will continue to depend on its ability to raise capital through equity and debt issuances and/or through strategic partnerships. The Company expects to continue to incur significant expenses and increasing operating losses for at least several years.

As of December 31, 2016, the Company had cash and cash equivalents of $35.0 million. The Company has no other sources of significant liquidity in place as of December 31, 2016. The Company expects that its existing cash and cash equivalents will fund its operations into the second half of 2017 based on the Company's 2017 operating plan. The Company has undertaken a strategic review of potential financing alternatives such as the sale of the company, a merger, a business combination, a strategic investment into the company, or a sale, license or disposition of assets of the Company. If the Company is unable to obtain additional funding on a timely basis, it may be required to curtail or terminate research and development activities under its collaboration agreement with Novartis, or to scale back, suspend or terminate its business operations.

As more fully discussed in Note 17 Subsequent Events, pursuant to management's plans, in March 2017 the Company entered into a series of transactions including the payoff of its note payable to Hercules Capital for $12.4 million. The Company sold and assigned all of its right, title and interest in and to its clinical product candidates CRLX101 and CRLX301 for proceeds of $1.5 million. The Company also agreed to sell and assign to Novartis all of its right, title and interest in and to the patent rights, know-how and third-party license agreements relating to its Dynamic Tumor Targeting Platform technology for proceeds of $6.0 million, whereby the proceeds from this asset sale are to be received upon closing of the transaction. The Company also entered into a Stock Purchase Agreement with Daré Biosciences, Inc., which if approved by the shareholders, will be consummated by an exchange of common stock shares and no cash consideration paid or received.

With exception of the payoff of the note payable and the sale of the clinical product candidates, these transactions are subject to certain closing conditions. There can be no assurances that these transactions will be consummated prior to the exhaustion of the Company's cash and cash equivalent resources, if at all.

The foregoing matters give rise to substantial doubt about the Company's ability to continue as a going concern. The accompanying financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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 (Waltham, 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, 2016 and 2015, the Company had restricted cash of $230,000 and $347,000, respectively. The restricted cash balances were used to collateralize stand-by letters of credit issued by the Company as a security deposit for its current and former facility leases. The balance at December 31, 2016, was with respect to the Company’s current facility lease which is scheduled to expire in February 2021. The balance at December 31, 2015, includes the balance for the current facility lease and the Company’s former facility lease which was scheduled to expire in February 2016 but was terminated early on December 31, 2015. 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, 2016 and 2015, the Company has not recorded an impairment charge for its long-lived assets.

Revenue Recognition —

Collaborative Research and Development and Multiple-Element Arrangements

The Company has entered into a collaboration arrangement with a strategic partner for the development and commercialization of product candidates utilizing the Company's technologies. The agreement provides for multiple deliverables by the Company (for example, license rights, research and development services and manufacturing of clinical materials) in exchange for consideration to the Company of a combination of non-refundable upfront fees, research and development funding, payments based upon achievement of clinical development or other milestones and royalties in the form of designated percentages of product net sales.

Revenue is recognized when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed and determinable and collection is reasonably assured. Multiple-element arrangements, such as license and development agreements, are analyzed to determine whether the deliverables can be separated or whether they must be accounted for as a single unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit. When the Company determines that an arrangement should be accounted for as a single unit of accounting, it must determine the period over which the performance obligations will be performed, and revenue will be recognized over the performance period.

Deferred Revenue

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized within one year following the balance sheet date are classified as non-current deferred revenue.

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.

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 credit s. 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 liabilities 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, 2016 and 2015, the Company had approximately $0.7 million and $0.6 million, respectively, of total unrecognized tax benefits, which would affect income tax expense if recognized, before consideration of its valuation allowance. During fiscal year 2016, the Company did not make any payment of interest and penalties on unrecognized tax benefits. In addition, there was nothing accrued for in the consolidated balance sheets for the payment of interest and penalties at December 31, 2016.

Guarantees and Indemnification — As permitted under Delaware law, the Company indemnifies its officers and directors 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. During the year ended December 31, 2016, the Company did not experience any losses related to these indemnification obligations. The Company does not expect significant claims related to these indemnification obligations, and consequently, has concluded the fair value of these obligations is not material. Accordingly, as of December 31, 2016 no amounts have been accrued related to such indemnification provisions.

Recent Accounting Pronouncements — In November 2016, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update 2016-18, "Statement of Cash Flows - Restricted Cash (Topic 230)". This new standard requires companies to include amounts generally described as restricted cash and restricted cash equivalents in cash and cash equivalents when reconciling beginning-of-period and end-of-period total amounts shown on the statement of cash flows. This guidance is effective for annual and interim reporting periods beginning after December 15, 2017, and required retrospective application. The Company is currently evaluating the effect this standard will have on its consolidated financial statements and related disclosures.

In August 2016, the FASB issued Accounting Standards Update 2016-15, "Statement of Cash Flows (Topic 230)" ("ASU 2016-15"). ASU 2016-15 provides guidance to clarify how cash payments for debt prepayment or debt extinguishment costs are to be classified in the statement of cash flows. The standard is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company is currently evaluating the effect this standard will have on its consolidated financial statements and related disclosures.

In March 2016, the FASB issued Accounting Standards Update 2016-09, "Compensation – Stock Compensation (Topic 718)" ("ASU 2016-09"). ASU 2016-09 is intended to simplify various aspects of how share-based payments are accounted for and presented in financial statements. The standard is effective prospectively for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2016, with early adoption permitted. For amendments that are to be applied on a modified retrospective basis, a cumulative-effect adjustment will be calculated on the first day of the fiscal year of adoption, which will be recorded in retained earnings. The Company has early adopted ASU 2016-09 for its quarter ended December 31, 2016. As a result of the Company's adoption of ASU 2016-09, it will track option deductions in its net operating loss deferred tax asset on a modified retrospective basis, and has included the option deductions in the December 31, 2016 deferred tax assets. In addition, the Company's policy has been to estimate forfeitures as of the grant date. The Company will continue to maintain its policy to estimate forfeiture as of the grant date in the future. The gross deferred tax asset and valuation allowance as of December 31, 2016, increased $163,000 as a result of the cumulative effect of adoption of ASU 2016-09. The adoption of ASU 2016-09 did not have a material impact on the Company's financial statements for the year ended and as of December 31, 2016.

In February 2016, the FASB issued Accounting Standards Update 2016-02, "Leases (Topic 842)" ("ASU 2016-02"), which provides new accounting guidance on leases. ASU 2016-02 requires lessees to recognize leases on their balance sheets, and leaves lessor accounting largely unchanged. The amendments in ASU 2016-02 are effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early application is permitted for all entities. ASU 2016-02 requires a modified retrospective approach for all leases existing at, or entered into after, the date of initial application, with an option to elect to use certain transition relief. The Company is currently evaluating the impact of this new standard on its consolidated financial statements and related disclosures.

In August 2014, the FASB issued Accounting Standards Update 2014-15, "Presentation of Financial Statements – Going Concern (Subtopic 205-40): 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, whethe r 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 May 2014, the FASB issued Accounting Standards Update 2014-09 (ASC 606), “Revenue from Contracts with Customers” (ASU 2015-09), which affects any entity that either enters into contracts with customers to transfer goods and services or enters into contracts for the transfer of nonfinancial assets. In August 2015, the FASB issued Accounting Standards Update 2015-14, “Revenue from Contracts with Customers” which defers the effective date of ASU 2014-09 for all entities by one year. ASU 2014-09, which has been codified with the Accounting Standards Codification as Topic 606, is now effective for public companies for annual reporting periods beginning after December 15, 2017, including interim periods within those reporting periods. ASC 606 outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. In addition, ASC 606 provides guidance on accounting for certain revenue-related costs including, but not limited to, when to capitalize costs associated with obtaining and fulfilling a contract. ASC 606 provides companies with two implementation methods. Companies can choose to apply the standard retrospectively to each prior reporting period presented (full retrospective application) or retrospectively with the cumulative effect of initially applying the standard as an adjustment to the opening balance of retained earnings of the annual reporting period that includes the date of initial application (modified retrospective application). Since ASU 2014-09 was issued, several additional Accounting Standards Updates have been issued and incorporated within ASC 606 to clarify various elements of the guidance. The Company plans to adopt this guidance on January 1, 2018. The Company has not yet determined whether it will utilize the full retrospective or the modified retrospective adoption method and continues to evaluate the impact that adoption will have on its consolidated 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,		
	2016	2015	2014
Net loss attributable to common stockholders — basic and diluted	$ (39,305)	$ (39,594)	$ (23,342)
Weighted-average number of common shares — basic and diluted	27,710,403	25,431,332	14,548,516
Net loss per share attributable to common stockholders — basic and diluted	$ (1.42)	$ (1.56)	$ (1.60)

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,		
	2016	2015	2014
Options to purchase common stock	4,020,288	3,454,926	2,126,176
Warrants to purchase common stock	365,564	300,564	128,663

4. PROPERTY AND EQUIPMENT

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

	As of December 31,	
	2016	2015
Laboratory equipment	$ 1,548	$ 1,314
Computer equipment	371	350
Office furniture and equipment	66	25
Leasehold improvements	75	33
	2,060	1,722
Less accumulated depreciation and amortization	(1,392)	(1,146)
Property and equipment, net	$ 668	$ 576

Depreciation and amortization expense for the years ended December 31, 2016, 2015, and 2014, was $261,000, $192,000, and $126,000, respectively.

5. ACCRUED EXPENSES

Accrued expenses consist of the following (in thousands):

	As of December 31,	
	2016	2015
Accrued clinical trial costs	$ 2,648	$ 2,631
Accrued contract manufacturing expenses	226	945
Accrued compensation and benefits	1,080	1,864
Accrued interest	82	136
Other accrued expenses	575	883
Total accrued expenses	$ 4,611	$ 6,459

6. LOAN AGREEMENTS

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. ("Hercules"). The proceeds were used to repay the Company's existing term loan facility with Lighthouse Capital Partners VI, L.P. ("Lighthouse Capital") and for general corporate and working capital purposes. At December 31, 2016, the Company had $13.1 million in principal outstanding under the Term Loan.

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 provided for up to three separate borrowings, the first of which was funded in the amount of $15.0 million on the Closing Date. On November 24, 2015, the Company drew a second tranche in the amount of $6.0 million. The Company elected not to commence a randomized Phase 2 clinical study of CRLX101 in combination with chemoradiotherapy on or prior to December 15, 2015, which was a condition of obtaining an additional tranche in an amount of up to $5.0 million. As a result, the Company is no longer eligible to borrow this amount under the Term Loan.

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 provided for interest-only payments on a monthly basis until December 31, 2015. Thereafter, payments are payable monthly in equal installments of principal and interest to fully amortize the outstanding principal over the remaining term of the loan, subject to recalculation upon a change in the prime rate. 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 1.0%. 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. The minimum future principal payments are as follows (in thousands):

Year Ending December 31,	
2017	$ 8,533
2018	4,544
Unamortized discount relating to warrants and deferred financing costs	(256)
Total	12,821
Less current portion	(8,382)
Long-term portion	$ 4,439

At the end of the loan term (whether at maturity, by prepayment in full or otherwise), the Company shall pay a final end of term charge to Hercules in the amount of 6.7% of the aggregate original principal amount advanced by Hercules. The amount of the end of term charge is being accrued over the loan term as interest expense. As of December 31, 2016, the Company has accrued $1.1 million related to the end of term charge, which has been classified as other long-term liabilities.

In connection with the Herc ules Loan Agreement, the Company issued to Hercules a warrant to purchase shares of the common stock of the Company at an exercise price of $6.05 per share. The warrant is exercisable for 171,901 shares of common stock. The warrant is exercisable until Jan uary 8, 2020. The Company estimated the fair value of the warrant for shares exercisable on the issue date in January 2015 to be $824,000. The value of the warrant was recorded as a discount to the loan. The fair value of the warrant was estimated on the d ate of issue for the exercisable shares at that date using the Black-Scholes option-pricing model. The following table shows the Black-Scholes assumptions used to value the warrant:

	January 8, 2015
Contractual life	5 years
Volatility rate	61%
Risk-free interest rate	1.5%
Expected dividends	—

At December 31, 2016, the Company's balance of unamortized deferred financing costs and unamortized debt discount were $0.1 million and $0.2 million, respectively. These costs are being amortized to interest expense using the effective interest method over the term of the loan.

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.

In December 2011, the Company entered into a loan and security agreement with Lighthouse Capital to borrow up to $10.0 million in one or more advances by December 31, 2012. In both March 2012 and August 2012, the Company borrowed $5.0 million under the loan and security agreement, for a total of $10.0 million. This amount was being repaid over 36 months beginning on December 1, 2012, at an interest rate of 8.25%. In addition, the Company was required to make an additional payment in the amount of $600,000 at the end of the loan term. The amount was accrued over the loan term as interest expense. The amount accrued as of December 31, 2014 was $574,000, and it was included in accrued expense in the Company's consolidated balance sheet. In January 2015, the Company repaid in full the amount outstanding under the Lighthouse Capital agreement, or $3.6 million, with the proceeds from the Hercules Loan Agreement.

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

7 . STOCKHOLDERS' EQUITY

Common Stock — In 2015, the Company issued 6,716,000 shares of common stock in connection with an underwritten public offering and 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.

Common Stock Purchase Agreement – On October 14, 2016, the Company entered into a common stock purchase agreement (the "Purchase Agreement") with Aspire Capital Fund, LLC ("Aspire Capital"), which provides that, upon the terms and subject to the conditions and limitations set forth therein, Aspire Capital is committed to purchase up to an aggregate of $20.0 million of shares of the Company's common stock over a term of 24 months from the execution of the Purchase Agreement. Immediately following the execution of the Purchase Agreement, the Company made an initial sale to Aspire Capital under the Purchase Agreement of 800,000 shares of common stock at a price of $1.25 per share, for gross proceeds of $1.0 million, and concurrently entered into a registration rights agreement with Aspire Capital registering the shares of the Company's common stock that have been and may be issued to Aspire Capital under the Purchase Agreement. In consideration for entering into the Purchase Agreement, the Company issued to Aspire Capital 700,000 shares of the Company's common stock as a commitment fee. The net proceeds of the Aspire Capital transaction, after offering expenses, to the Company were approximately $786,000. At December 31, 2016, up to $19.0 million of the Company's common stock that may be sold at the prevailing share price at the time of sale subject to conditions specified in the Purchase Agreement remains available.

Reserved Shares of Common Stock — The Company has reserved the following number of shares of common stock at December 31, 2016 and 2015:

	As of December 31,	
	2016	2015
Warrants to purchase common stock	365,564	300,564
Common stock options	4,020,288	3,995,876
Total	4,385,852	4,296,440

8. 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, 2016 and 2015, there were no 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. The 2014 Plan provides an annual increase in the number of shares available for grant on the first day of each calendar year beginning with the fiscal year ended December 31, 2015 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2024, equal to the lesser of (i) 1,000,000 shares of common stock, (ii) 4% of the number of outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors. As of December 31, 2016, there were 924,400 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, 2016 is presented below (Aggregate Intrinsic Value in thousands):

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value
Outstanding at January 1, 2016	3,454,926	$ 5.39	8.9	$ —
Granted	1,597,570	1.86		
Exercised	—			
Forfeited	(1,032,208)	4.12		
Outstanding at December 31, 2016	4,020,288	$ 4.31	8.4	$ —
Options exercisable at December 31, 2016	1,634,944	$ 5.41	7.7	$ —
Options vested and expected to vest at December 31, 2016	3,900,976	$ 4.33	8.4	$ —

The total intrinsic value of stock options exercised in the years ended December 31, 2016, 2015, and 2014 was $0, $0, and $161,000, respectively.

The weighted-average per share grant date fair value of options granted during 2016, 2015, and 2014 was $1.07, $3.22, and $3.33, respectively.

The Company has recorded stock-based compensation expense of $2.7 million, $2.4 million, and $885,000 during the years ended December 31, 2016, 2015, and 2014, respectively, wh ich is based on the number of awards ultimately expected to vest. As of December 31, 2016, there was $4.1 million of unrecognized compensation cost related to unvested stock-based compensation arrangements granted under the 2007 Plan and the 2014 Plan. Th e compensation is expected to be recognized over a weighted-average period of 2.02 years at December 31, 2016.

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

	As of December 31,		
	2016	2015	2014
Research and development	$ 1,098	$ 795	$ 317
General and administrative	1,657	1,580	568
Total	$ 2,755	$ 2,375	$ 885

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, 2016, 2015, and 2014 are as follows:

	December 31,		
	2016	2015	2014
Expected life	6 years	6 years	6 years
Risk-free interest rate	1.20%-2.32%	1.45%-2.02%	1.71%-2.00%
Expected volatility	61%-68%	51%-63%	54%-60%
Expected dividend rate	—%	—%	—%

The Company recorded stock-based compensation expense related to nonemployee awards of $77,000, $173,000, and $56,000 for the years ended December 31, 2016, 2015, and 2014, 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, 2016, 2015, and 2014 were as follows:

	December 31,		
	2016	2015	2014
Expected life	10 years	10 years	8 years
Risk-free interest rate	1.56%-2.43%	2.10%-2.25%	1.86%-2.53%
Expected volatility	60%-61%	60%-61%	56%-62%
Expected dividend rate	—%	—%	—%

During the year ended December 31, 2016, the Company granted nonemployee stock options to consultants for the purchase of 140,000 shares of the Company's common stock. The weighted-average exercise price and the weighted-average fair value of nonemployee stock options granted for the year ended December 31, 2016, was $1.08 per share and $0.46 per share, respectively. The fair value of the grants is being expensed over the vesting period of the options on a straight-line basis as the services are being provided. On September 4, 2015, nonemployee stock options to purchase 90,000 shares of the Company's common stock were converted to employee stock options upon the appointment of the Company's Chief Medical Officer who had been serving as a consultant to the Company until his appointment. The exercise price and the fair value of these stock options is $4.71 per share and $2.71 per share, respectively. The Company did not grant any nonemployee stock option grants in 2014.

In 2012, the Company granted options to purchase 60,934 common shares to an officer of the Company, now the Company's Chief Executive 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, 2016. 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 dir ectors 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 th e 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 Comp any'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. There are two six-month offerings per year. The first offering period under the 2014 ESPP began on July 1, 2015. The compensation expense related to the 2014 ESPP is included in the total stock-based compensation. The stock-based compensation expense related to the ESPP for the year ended December 31 , 2016 and 2015, was $24,000 and $27,000, respectively. There was no stock-based compensation related to the 2014 ESPP recorded for the year ended December 31, 2014.

9. 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, 2016 and 2015, are money market fund investments of $35.0 million and $75.3 million, 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 (unadjusted) in active markets that are accessible at the market date for identical unrestricted assets or liabilities.

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

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

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

		Fair Value Measurements Using		
	Carrying Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
December 31, 2016				
Money market funds	$ 34,950	$ —	$ 34,950	$ —
December 31, 2015				
Money market funds	$ 75,325	$ —	$ 75,325	$ —

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, 2016 and 2015, there have been no transfers between levels.

10. INCOME TAXES

Significant components of the Company's deferred taxes at December 31, 2016, and 2015 are as follows:

	2016	2015
Net operating loss carryforwards	$ 42,211	$ 35,797
Research and development credit carryforwards	2,486	2,066
Capitalized costs	4,453	3,977
Capitalized research and development costs	24,923	17,715
Other	1,878	903
Total deferred tax assets	75,951	60,458
Valuation allowance	(75,951)	(60,458)
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 2016 and 2015 by approximately $15.5 million and $15.6 million, respectively, due to the increases in the deferred tax assets by the same amounts. The increases are mainly attributable to operating losses generated in the period.

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,	
	2016	2015
Federal income tax expense at statutory rate	34.0%	34.0%
State income tax, net of federal benefit	5.0%	5.0%
Permanent differences	(0.6%)	(0.5%)
Research and development credit	1.1%	0.9%
Stock compensation	(0.5%)	(0.7%)
Other	0.2%	0.4%
Change in valuation allowance	(39.2%)	(39.1%)
Effective income tax rate	0.0%	0.0%

At December 31, 2016, the Company has approximately $109.7 million of federal and $90.2 million of state net operating loss carryforwards that expire at various dates through 2036. At December 31, 2016, the Company has approximately $1.7 million of federal and $1.1 million of state research and development credit carryforwards that expire at various dates through 2036 for federal credits and 2031 for state credits.

At December 31, 2015, the Company has approximately $93.7 million of federal and $74.1 million of state net operating loss carryforwards that expire at various dates through 2035. At December 31, 2015, the Company has approximately $1.4 million of federal and $0.9 million of state research and development credit carryforwards that expire at various dates through 2035 for federal credits and 2030 for state credits.

The Company has early adopted the provisions of ASU 2016-09, Compensation – Stock Compensation (Topic 718 Improvements to Employee Share-Based Payment Accounting), for its quarter ended December 31, 2016. ASU 2016-09 requires companies to include the benefit of an option deduction in its net operating loss carryforward deferred tax asset. Prior to its adoption of ASU 2016-09, the Company's excess tax benefits associated with option deductions were maintained in the Company's APIC pool of windfall tax benefits, which was tracked off balance sheet and not included in its deferred tax assets. As a result of the Company's adoption of ASU 2016-09, it will track option deductions in its net operating loss deferred tax asset on a modified retrospective basis, and has included the option deductions in the December 31, 2016 deferred tax assets. The gross deferred tax asset and valuation allowance as of December 31, 2016 increased $163,000 as a result of the cumulative effect of adoption of ASU 2016-09. The Company has not recast its December 31, 2015 and December 31, 2014 deferred tax assets or its rate reconciliation, and therefore the option deductions in 2015 and 2014 are not included in the net operating loss deferred tax asset as originally reported. Since the

Company has historically maintained a full valuation allowance on its net worldwide deferred tax asset, there is no net impact to retained earnings from the adoption of ASU 2016-09.

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 and 383 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 amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed numerous financings since its inception which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

The Company files income tax returns in the United States, the Commonwealth of Massachusetts, and Australia. The tax years 2008 through 2016 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, 2016 and 2015, the Company had approximately $0.7 million and $0.6 million, respectively, of total unrecognized tax benefits, which would affect income tax expense if recognized, before consideration of the Company's valuation allowance. During fiscal year 2016, the Company did not make any payment of interest and penalties on unrecognized tax benefits. In addition, there was nothing accrued for in the consolidated balance sheets for the payment of interest and penalties at December 31, 2016.

11. COMMITMENTS

Facility Lease — On July 9, 2015, the Company entered into a noncancelable operating lease with a third party for office, laboratory and vivarium space that is scheduled to expire in February 2021, subject to a three-year renewal option. The lease agreement includes base rent escalation over the lease term which will be amortized on a straight-line basis over the lease term with the resulting deferred liability recorded in other current and long-term liabilities. The resulting deferred liability recorded in other current and long-term liabilities as of December 31, 2016 was $153,000. 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. Rent expense under this lease was $728,000 for the year ended December 31, 2016.

The Company amended the lease, effective March 29, 2017, to remove 1,753 square feet from the lease, which space was previously used for vivarium and vivarium support purposes. The Company's base rent and share in expenses and property taxes have been reduced based on the revised pro-rata allocation of the premises.

Future minimum lease payments under the non-cancelable operating lease are as follows (in thousands):

Years Ending December 31,	Operating Leases
2017	$ 690
2018	738
2019	786
2020	830
2021	140
Total	$ 3,184

Potential Payments upon Termination or Change in Control — On March 19, 2017, the Company entered into retention agreements with certain executive officers. These retention agreements supersede the provisions of such executive officers' employment agreements and retention letters with the Company providing for post-separation benefits, and provide for certain lump sum payments ranging from 6 to 18 months of salary, plus health and dental insurance coverage, while also providing the covered executives with a cash bonus upon completion of a change in control. Under the terms of the retention agreements, the Company may be required to pay up to approximately $1.8 million .

12. LICENSING AGREEMENTS

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 spec ified 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 paid Calando a $250,000 clinical development milestone which was recorded in December 2014 upon initiation of the Phase 1/2a clinical trial for CRLX301. The Company may be required to make additional milestone payments to Calando of up to $17.8 million, in the aggregate, upon the achievement of specified regulatory and commercial milestones and pay royalty payments ranging from low-to mid-single digits on commercial sales.

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. The trustee's last deadline was February 7, 2017. To our knowledge, no sale of such rights was ever consummated.

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, $30,000, and $25,000 for the years ended December 31, 2016, 2015, and 2014, respectively.

Massachusetts Institute of Technology License — The Company delivered a notice of termination which became effective on November 1, 2015, with respect to the Company's license agreement with the Massachusetts Institute of Technology ("MIT"). The agreement as amended required the Company to pay MIT nonrefundable annual license maintenance fees that increased each year beginning in 2015. In connection with this agreement, the Company recorded research and development expense for annual maintenance fees of $50,000 for the year ended December 31, 2015, and $10,000 in the year ended December 31, 2014.

13. 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 $292,000, $264,000, and $163,000 to the 401(k) Plan for the years ended December 31, 2016, 2015, and 2014, respectively.

14. 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, were $39,000. 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.

15. REVENUE

In October 2016, the Company entered into a research collaboration agreement with Novartis pursuant to which the Company granted to Novartis certain exclusive, world-wide licenses to the Company's intellectual property relating to its platform technology and know-how. Under the collaboration, the Company and Novartis agreed to collaborate, over an initial research term of two years, with respect to the pre-clinical development of nanoparticle drug conjugates comprised of the Company's proprietary polymer covalently linked to Novartis-selected active pharmaceutical ingredients for up to five targets to be agreed upon by the Company and Novartis. Novartis may extend the initial research term by up to two additional one-year periods. In October 2016, the Company received a $5.0 million upfront payment under the collaboration which it will recognize on a straight-line basis over the initial term of the collaboration. The Company will also receive funding from Novartis for up to five full-time employees of the Company to be engaged in activities under the collaboration during the research term. For the year ended December 31, 2016, the Company

recognized revenue of $ 507 ,000 in connection with the upfront fee and $259,000 in connection with the funding for activities performed under the collaboration during the research term .

In 2013, the Company entered into material transfer agreements with two separate biopharmaceutical companies to conduct feasibility studies using the Company's proprietary technology. The Company recognized revenue of $80,000 for the year ended December 31, 2014, in connection with these material transfer agreements. The Company had no revenue for the years ended December 31, 2016 and 2015 related to these agreements.

16. 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, 2016			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ —	$ —	$ —	$ 766
Operating expenses:				
Research and development	9,770	7,522	7,089	3,184
General and administrative	3,118	2,773	2,374	2,090
Total operating expenses	12,888	10,295	9,463	5,274
Other income (expense):				
Interest income	16	25	25	20
Interest expense	(670)	(589)	(521)	(457)
Total other income (expense) — net	(654)	(564)	(496)	(437)
Net loss attributable to common stockholders	$ (13,542)	$ (10,859)	$ (9,959)	$ (4,945)
Net loss per share attributable to common stockholders:				
Basic and diluted	$ (0.49)	$ (0.40)	$ (0.36)	$ (0.17)
Weighted-average common shares outstanding:				
Basic and diluted	27,362,643	27,363,965	27,383,376	28,724,083

	Year Ended December 31, 2015			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	5,021	6,678	7,092	7,157
General and administrative	2,681	2,717	2,954	2,872
Total operating expenses	7,702	9,395	10,046	10,029
Other income (expense):				
Interest income	3	1	4	2
Interest expense	(721)	(513)	(509)	(689)
Total other income (expense) — net	(718)	(512)	(505)	(687)
Net loss attributable to common stockholders	$ (8,420)	$ (9,907)	$ (10,551)	$ (10,716)
Net loss per share attributable to common stockholders:				
Basic and diluted	$ (0.41)	$ (0.37)	$ (0.39)	$ (0.39)
Weighted-average common shares outstanding:				
Basic and diluted	20,350,557	26,690,673	27,307,103	27,346,780

17. SUBSEQUENT EVENTS

In February 2017, the Company announced that its board of directors initiated a review of strategic alternatives that could result in changes to the Company's business strategy and future operations. As part of this process, the board determined to review alternatives with the goal of maximizing stockholder value, including a potential sale of the Company, a reverse merger, a business combination or a sale, license or other disposition of company assets.

The Company entered into a payoff letter dated as of March 17, 2017 with Hercules pursuant to which the Company agreed to pay off and thereby terminate the Hercules Loan Agreement. Pursuant to the payoff letter, the Company paid, on March 20, 2017, a total of $12.4 million to Hercules, representing the principal, accrued and unpaid interest, fees, costs and expenses outstanding under the Hercules Loan Agreement in repayment of its outstanding obligations under the Hercules Loan Agreement. This payoff amount included a final end of term charge to Hercules in the amount of $1.4 million, representing 6.7% of the aggregate original principal amount advanced by Hercules. As of December 31, 2016, the Company has accrued $1.1 million of the end of term charge. Upon the payment of the $12.4 million pursuant to the payoff letter, all outstanding indebtedness and obligations owed to Hercules under the Loan Agreement were deemed paid in full, and the Loan Agreement was terminated.

On March 19, 2017, the Company entered into an a sset p urchase a greement (the "Novartis Asset Purchase Agreement") with Novartis. Under the Novartis Asset Purchase Agreement the Company agreed to sell and assign to Novartis all of the Company's rig ht, title and interest in and to the patent rights, know-how and third-party license agreements relating to the Company's proprietary Dynamic Tumor Targeting Platform (the " Platform ") . At the closing of the Novartis transaction, Novartis will be obligated to pay a purchase price of $6.0 million. Consummation of the Novartis transaction is subject to certain closing conditions, including, among other things, approval by the Company's stockholders.

On March 19, 2017, the Company also entered into an asset purchase agreement (the "BlueLink Asset Purchase Agreement) with BlueLink Pharmaceuticals, Inc. ("BlueLink"). Under the BlueLink Asset Purchase Agreement the Company sold and assigned to BlueLink all of the Company's right, title and interest in and to its clinical product candidates CRLX101 and CRLX301 (the "Products"). The Company also transferred and assigned to BlueLink the accompanying intellectual property rights and know-how to the Products. On March 21, 2017, BlueLink paid the purchase price of $1.5 million. Also in connection with the BlueLink Asset Purchase Agreement, the Company and BlueLink entered into a license agreement in favor of BlueLink, pursuant to which the Company agreed to grant to BlueLink an exclusive, worldwide, perpetual, sublicensable right and license, under the Platform, to research, develop and commercialize the Products. Pursuant to the Novartis Asset Purchase Agreement between the Company and Novartis, Novartis will assume the BlueLink License upon the closing of the Novartis transaction.

On March 19, 2017, the Company also entered into a stock purchase agreement (the "Stock Purchase Agreement")with Daré Bioscience, Inc. ("Daré"), and the holders of capital stock and securities convertible into capital stock of Daré named therein ("Selling Stockholders"), pursuant to which, among other things, the Selling Stockholders agreed to sell to the Company, and the Company agreed to purchase from the Selling Stockholders, all of the outstanding shares of capital stock, including those issuable upon conversion of convertible securities, of Daré (the "Daré Transaction"). Immediately following the closing of the Daré Transaction, the Selling Stockholders are expected to own between approximately 51% and 70% (depending on the net cash positions of the Company and Daré at closing) of the outstanding equity securities of Cerulean Pharma Inc. Consummation of the Daré Transaction is subject to certain closing conditions, including, among other things, approval by the Company's stockholders. The exchange ratio, and therefore fair value of exchange consideration, are indeterminable at this time, and as such the full disclosures required under Accounting Standards Codification 805, Business Combinations, are impracticable. The Stock Purchase Agreement contains certain termination rights for both the Company and Daré, and further provides that, upon termination of the Stock Purchase Agreement under specified circumstances, the Company may be required to pay Daré a termination fee of $0.3 million, or Daré may be required to pay the Company a termination fee of $0.45 million. There can be no assurances that the Daré Transaction will be consummated.

On March 20, 2017, the Company announced a restructuring including the elimination of approximately 58% of its workforce, to a total of eight full-time equivalent employees, under a plan expected to be completed during the second quarter of 2017.

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, 2016.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(e) under the Exchange Act.

Under the supervision and with the participation of management, including our principal executive officer and principal financial officer, we conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control-Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, management concluded that, as of December 31, 2016, our internal control over financial reporting was effective.

This annual report does not include an attestation report of our registered public accounting firm on internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth 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, 2016 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Effective March 29, 2017, we entered into an amendment, or the First Lease Amendment, to the lease dated July 9, 2015 for the premises comprising the Company's headquarters at 35 Gatehouse Drive, Waltham, Massachusetts, or the Lease. Pursuant to the First Lease Amendment, we and AstraZeneca Pharmaceuticals agreed that 1,753 square feet of the premises originally subject to the Lease, which was previously used for vivarium and vivarium support purposes, would no longer be subject to the Lease, thereby reducing the leased premises to 21,239 square feet of office and laboratory space. Our monthly base rent, pro-rata contribution towards facility-wide overhead costs, and parking space allocation have all been reduced based on the revised pro-rata allocation of the Company's use of the reduced premises subject to the Lease.

P ART III

I tem 10. Directors, Executive Officers and Corporate Governance

Christopher D. T. Guiffre, age 48, has served as our President and Chief Executive Officer since March 2015. He previously served as our Chief Operating Officer and 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.

Gregg D. Beloff , age 48, has served as our Interim Chief Financial Officer since May 2015. Mr. Beloff has been a Managing Director of Danforth Advisors, a consulting firm specializing in providing financial and strategic support to life sciences companies, since April 2011. In addition to consulting for clients, Mr. Beloff previously served as the chief financial officer of two public and three privately held companies. In these roles, he has managed finance, accounting, corporate communications, human resources, information technology, facilities, legal, intellectual property, business development, and manufacturing functions. Mr. Beloff holds a J.D. from the University of Pittsburgh School of Law, an M.B.A. from Carnegie Mellon University, and a B.A. in History from Middlebury College.

Adrian M. Senderowicz, M.D. , age 53, has served as our Chief Medical Officer and Senior Vice President since September 2015. Prior to joining Cerulean, Dr. Senderowicz worked at Ignyta, Inc., a public precision oncology biotechnology company, as Chief Medical Officer and Senior Vice President, Clinical Development and Regulatory Affairs from August 2014 to February 2015, and as Clinical and Regulatory Strategy Officer from February 2015 to April 2015. Previously, he was Vice President, Global Regulatory Oncology at Sanofi, a biopharmaceutical company, from September 2013 to August 2014, and Chief Medical Officer at Tokai Pharmaceuticals, Inc., a biopharmaceutical company focused on prostate cancer treatment, from August 2012 to March 2013. From August 2008 to March 2012, Dr. Senderowicz held positions of increasing responsibility at AstraZeneca, a global biopharmaceutical company, including most recently as Senior Medical Director, Oncology Clinical Development. Before his tenure at AstraZeneca, Dr. Senderowicz held a variety of leadership positions at the U.S. Food and Drug Administration Division of Oncology Drug Products in the Center for Drug Evaluation and Research and a variety of clinical and research positions with the National Cancer Institute/National Institutes of Health (NCI), including Investigator and Chief, Molecular Therapeutics Unit. He currently serves as a director of Puma Biotechnology, Inc., a publicly traded biopharmaceutical company. He completed his Internal Medicine residency training at the Icahn School of Medicine at Mount Sinai, and a Clinical Oncology Fellowship at the NCI. Dr. Senderowicz holds an M.D. from the School of Medicine at the Universidad de Buenos Aires in Argentina.

Scott Eliasof, Ph.D. , age 58, has served as our Chief Scientific Officer and Senior Vice President since October 2016. He previously served as our Vice President, Research and lead our research team since 2007. Prior to joining Cerulean, he was the director of the Chemical Biology Platform at the Broad Institute, directing a multi-disciplinary team of professional scientists and technicians in the fields of synthetic chemistry, analytical chemistry, high-throughput screening, computational science, and software engineering. Prior to joining the Broad Institute, Dr. Eliasof worked at Millennium Pharmaceuticals, where he managed scientific teams in cellular biology, molecular biology, neuroscience, and bioinformatics for a large-scale genomics-based drug discovery program. Earlier in his career, Dr. Eliasof was at Neurocrine Biosciences, Inc., where he played a key role in the exploration of glutamate transporters in the field of stroke and neurological disorders. Dr. Eliasof earned his B.S. from the Massachusetts Institute of Technology in electrical engineering, Ph.D. from the University of California at Berkeley in neuroscience, and completed his post-doctoral fellowship at the Vollum Institute in Portland, Oregon.

Alejandra V. Carvajal, age 43, has served as our Vice President and General Counsel since September 2014. Prior to joining Cerulean, and beginning in 2004, Ms. Carvajal held a variety of positions at Millennium: The Takeda Oncology Company, or Millenium, including most recently as Associate General Counsel. Ms. Carvajal joined Millennium as a senior attorney and enjoyed over ten years of increasing responsibilities relating to all aspects of oncology drug development. Prior to joining Millennium, Ms. Carvajal was an attorney with the law firms Day, Berry & Howard, and Hill & Barlow. Ms. Carvajal received a B.A. cum laude from Harvard University and a J.D. cum laude from Georgetown University Law Center.

The remaining information required by this Item 10 will be contained in our proxy statement for our 2017 annual meeting of stockholders and is incorporated herein by reference.

I tem 11. Executive Compensation

The information required by this Item 11 will be contained in our proxy statement for our 2017 annual meeting of stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be contained in our proxy statement for our 2017 annual meeting of stockholders and is incorporated herein by reference.

I tem 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item 13 will be contained in our proxy statement for our 2017 annual meeting of stockholders and is incorporated herein by reference.

I tem 14. Principal Accountant Fees and Services

The information required by this Item 14 will be contained in our proxy statement for our 2017 annual meeting of stockholders and is incorporated herein by reference.

P ART IV

I tem 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
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 31, 2017

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*	President, Chief Executive Officer, and Director *(Principal Executive Officer)*	March 31, 2017
/s/ Gregg D. Beloff *Gregg D. Beloff*	Interim Chief Financial Officer *(Principal Financial Officer)*	March 31, 2017
/s/ James E. O'Neill *James E. O'Neill*	Corporate Controller *(Principal Accounting Officer)*	March 31, 2017
/s/ William H. Rastetter *William H. Rastetter, Ph.D.*	Director	March 31, 2017
/s/ Stuart A. Arbuckle *Stuart A. Arbuckle*	Director	March 31, 2017
/s/ Alan L. Crane *Alan L. Crane*	Director	March 31, 2017
/s/ Paul A. Friedman *Paul A. Friedman, M.D.*	Director	March 31, 2017
/s/ Susan L. Kelley *Susan L. Kelley, M.D.*	Director	March 31, 2017
/s/ William T. McKee *William T. McKee*	Director	March 31, 2017
/s/ David R. Parkinson *David R. Parkinson, M.D.*	Director	March 31, 2017
/s/ David R. Walt *David R. Walt, Ph.D.*	Director	March 31, 2017

Exhibit Index

Exhibit Number	Description of Exhibit	Incorporated By Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
2.1*	Stock Purchase Agreement dated as of March 19, 2017, entered into by and among the Registrant, Daré Bioscience, Inc. and equityholders of Daré Bioscience, Inc. named therein	8-K	001-36395	March 20, 2017	2.1	
2.2*	Asset Purchase Agreement dated as of March 19, 2017, entered into by and between the Registrant and Novartis Institutes for BioMedical Research, Inc.	8-K	001-36395	March 20, 2017	2.2	
2.3*	Asset Purchase Agreement dated as of March 19, 2017, entered into by and between the Registrant and BlueLink Pharmaceuticals, Inc.	8-K	001-36395	March 20, 2017	2.3	
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	
3.3	Amendment to Amended and Restated By-laws	8-K	001-36395	March 20, 2017	3.1	
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	
10.8†	IT-101 Agreement, dated as of June 23, 2009, between the Registrant and Calando Pharmaceuticals, Inc.	S-1	333-194442	March 10, 2014	10.10	
10.10†	Platform Agreement, dated as of June 23, 2009, between the Registrant and Calando Pharmaceuticals, Inc.	S-1	333-194442	March 10, 2014	10.11	
10.11†	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	
10.12	Second Series D Convertible Preferred Stock Purchase Agreement, dated November 30, 2012, as amended	S-1	333-194442	March 10, 2014	10.13	
10.13	Warrant, dated January 8, 2015, issued to Hercules Technology Growth Capital, Inc.	8-K	001-36395	January 8, 2015	4.1	
10.14#	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors	S-1	333-194442	March 10, 2014	10.16	
10.15	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	

10.16	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
10.17	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
10.18#	Amended and Restated Employment Agreement dated March 27, 2015 between the Registrant and Christopher D. T. Guiffre	S-1	333-202917	March 30, 2015	10.26
10.19	Lease, dated July 9, 2015, between the Registrant and AstraZeneca Pharmaceuticals Limited Partnership	10-Q	001-36395	August 6, 2015	10.1
10.20#	Consulting Agreement, dated May 27, 2015, between the Registrant and Danforth Advisors LLC	10-Q	001-36395	August 6, 2015	10.2
10.21#	Employment Agreement, dated September 4, 2015, between the Registrant and Adrian Senderowicz, M.D.	10-Q	001-36395	November 16, 2015	10.3
10.22#	Employment Agreement, dated September 23, 2014, between the Registrant and Alejandra V. Carvajal	10-K	001-36395	March 10, 2016	10.26
10.23#	Amendment to Employment Agreement dated December 1, 2015, between the Registrant and Alejandra V. Carvajal	10-K	001-36395	March 10, 2016	10.27
10.24#	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
10.25#	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
10.26#	Amendment, dated May 27, 2016, to consulting agreement, dated as of May 27, 2015, between the Registrant and Danforth Advisors LLC	10-Q	001-36395	August 4, 2016	10.1
10.27#	Amendment, dated November 1, 2016, to consulting agreement, dated as of May 27, 2015, between the Registrant and Danforth Advisors LLC	10-Q	001-36395	November 3, 2016	10.1
10.28#	Summary of Non-employee Director Compensation Policy	10-Q	001-36395	November 3, 2016	10.2
10.29	Common Stock Purchase Agreement, dated October 14, 2016 between the Registrant and Aspire Capital Fund, LLC	8-K	001-36395	October 18, 2016	99.1
10.30	Registration Rights Agreement, dated October 14, 2016, between the Registrant and Aspire Capital Fund, LLC	8-K	001-36395	October 18, 2016	99.2
10.31 †	Research Collaboration Agreement, dated October 18, 2016, between the Registrant and Novartis Institutes for BioMedical Research, Inc.	10-Q	001-36395	November 3, 2016	10.3
10.32#	Form of Retention Letter between the Registrant and each of its executive officers	8-K	001-36395	November 8, 2016	99.1

10.33	Support Agreement dated as of March 19, 2017, entered into by and among the Registrant, Daré Bioscience, Inc. and shareholders of Cerulean Pharma Inc. named therein.	8-K	001-36395	March 20, 2017	10.1	
10.34	License Agreement dated as of March 19, 2017, entered into by and between the Registrant and BlueLink Pharmaceuticals, Inc.	8-K	001-36395	March 20, 2017	10.2	
10.35	Payoff Letter dated as of March 17, 2017, entered into by and between the Registrant and Hercules Capital, Inc. (formerly known as Hercules Technology Growth Capital, Inc.)	8-K	001-36395	March 20, 2017	10.3	
10.36#	Retention Agreement dated as of March 19, 2017, entered into by and between the Registrant and Christopher D. T. Guiffre	8-K	001-36395	March 20, 2017	10.4	
10.37#	Retention Agreement dated as of March 19, 2017, entered into by and between the Registrant and Adrian Senderowicz	8-K	001-36395	March 20, 2017	10.5	
10.38#	Retention Agreement dated as of March 19, 2017, entered into by and between the Registrant and Alejandra Carvajal	8-K	001-36395	March 20, 2017	10.6	
10.39	First Amendment of Lease, dated March 29, 2017, to Lease dated July 9, 2015, between the Registrant and AstraZeneca Pharmaceuticals Limited Partnership					X
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					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Label Linkbase Document					X
101.PRE	XBRL Taxonomy Presentation Linkbase Document					X

* All schedules (or similar attachments) have been omitted from this filing pursuant to Item 601(b)(2) of Regulation S-K. The Registrant will furnish copies of any schedules to the Securities and Exchange Commission upon request.

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

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

FIRST AMENDMENT OF LEASE

THIS FIRST AMENDMENT OF LEASE (the " **Amendment** ") is made and entered into as of March 29, 2017 (the " **Amendment Effective Date** ") by and between **ASTRAZENECA PHARMACEUTICALS LP** (" **Landlord** ") and **CERULEAN PHARMA INC.** (" **Tenant** ") .

RECITALS

A. Landlord and Tenant are parties to that certain Lease dated as of July 9, 2015 (the " **Existing Lease** ") whereby Tenant leases certain space in the buildings and facilities commonly known as 35 Gatehouse Drive, Waltham, Massachusetts (" **Landlord's Property** "), which leased space currently consists of 12,147 square feet of rentable office space located on Level 2 of Building D (the " **D2 Space** "), 9,092 square feet of rentable laboratory space located on Level 3 of Building C (the " **C3 Space** ") and 1,753 square feet of rentable space located in the vivarium and vivarium support space on Level 2 of Building C (the " **Vivarium Space** ", and collectively with the D2 Space and C3 Space, the " **Original Premises** "), all as more particularly set forth in the Existing Lease.

B. Landlord and Tenant desire to release the Vivarium Space from the Existing Lease as of the Amendment Effective Date.

C . The Existing Lease, as amended by this First Amendment of Lease, shall be referred to herein as the " **Lease** "; and capitalized terms not otherwise defined herein shall have their respective definitions set forth in the Existing Lease.

NOW, THEREFORE , in consideration of the above recitals which by this reference are incorporated herein, the mutual covenants and conditions contained herein and other valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant agree as follows:

1. **Premises; Landlord's Equipment; Surrender of Vivarium Space.**

a. Effective as of the Amendment Effective Date: (i) the Vivarium Space shall be released from the Existing Lease, (ii) the D2 Space and C3 Space shall together constitute the "Premises" for all purposes under the Lease and (iii) the "Leasable Square Footage of the Premises" set forth in Section 3C of the Summary of Basic Terms in Existing Lease shall be deemed to be **21,239** square feet.

b. Effective as of the Amendment Effective Date, the term "Landlord's Equipment" shall include the equipment owned by Landlord and located in the D2 Space and C3 Space only.

c. Tenant hereby acknowledges that, unless Tenant shall be permitted to remain in occupancy of the Vivarium Space under a separate written agreement with Landlord, Tenant shall be deemed in holdover with respect to the Vivarium Space under the Lease if Tenant fails to surrender possession of the Vivarium Space by the Amendment Effective Date, and in such event Landlord shall have all rights and remedies at law, in equity and under the Lease with respect to such holdover in the Vivarium Space.

2. **Base Rent; Tenant's Share Taxes and Operating Costs.**

a. Effective as of the Amendment Effective Date, Section 8 of the Summary of Basic Terms shall be modified to provide that the Base Rent for the Premises shall be as set forth in the following chart (pro-rated for partial months):

Period	Rent per rsf	Annual Base Rent	Monthly Base Re
Amendment Effective Date – February 28, 2018	$26.29	$558,285.00	$46,523.75
March 1, 2018 – February 28, 2019	$28.99	$615,765.00	$51,313.75
March 1, 2019 – February 28, 2020	$31.16	$661,749.00	$55,145.75
March 1, 2020 – February 28, 2021	$33.32	$707,733.00	$58,977.75

b. Effective as of the Amendment Effective Date, "Tenant's Share" shall be modified to mean **7.14%** being the amount (expressed as a percentage) equal to (a) the aggregate Leasable Square Footage of the Premises (i.e. the D2 Space and C3 Space) divided by (b) the Leasable Square Footage of the Building (rounded to the nearest one-hundredth of one percent (0.01%)).

c. Effective as of the Amendment Effective Date, the "Water Service Charge" set forth in Section 6.1(c) of the Existing Lease shall be deemed to be **$2,619.48** per month ($1.48/rsf per annum).

3. **Parking.** Effective as of the Amendment Effective Date, the provisions of the Existing Lease regarding Tenant's parking rights shall be modified as follows:

a. Section 7 of the Summary of Basic Terms in the Existing Lease shall be replaced with the following:

"7. Tenant's Parking Allocation: Fifty-three (53) unassigned parking spaces (2.5 spaces per 1,000 leasable square feet of the Premises), subject to the provisions of Section 2.3."

b. The definition of "Specified Number" in Article I of the Existing Lease shall be modified by replacing the number "fifty-eight (58)" with the number "fifty-three (53)".

4. **Miscellaneous.**

a. Effective as of the date hereof, Section 2.9 of the Existing Lease shall be deleted and of no further force or effect.

b. This Amendment sets forth the entire agreement between the parties with respect to the matters set forth herein. There have been no additional oral or written representations or agreements. Under no circumstances shall Tenant be entitled to any Rent abatement, improvement allowance, leasehold improvements, or other work to the Premises, or any similar economic incentives that may have been provided Tenant in connection with entering into the Existing Lease, unless specifically set forth in this Amendment.

c. Except as is expressly modified or amended herein, the provisions, conditions and terms of the Existing Lease shall remain unchanged and in full force and effect.

d. In the case of any inconsistency between the provisions of the Existing Lease and this Amendment, the provisions of this Amendment shall govern and control.

e. Landlord has delivered a copy of this Amendment to Tenant for Tenant's review only and the delivery of it does not constitute an offer to Tenant or an option. Landlord and Tenant shall not be bound by this Amendment until Landlord and Tenant have executed and delivered the same to the other party.

f. This Amendment is executed as a sealed instrument and in multiple counterparts, all copies of which are identical, and any one of which is to be deemed to be complete in itself and may be introduced in evidence or used for any purpose without the production of any other copy.

g. Tenant and Landlord hereby represent to each other that Landlord and Tenant have dealt with no broker in connection with this Amendment. Tenant and Landlord agree to indemnify and hold each other, its trustees, members, principals, beneficiaries, partners, officers, directors, employees, mortgagee(s) and agents, and the respective principals and members of any such agents harmless from all claims of any other brokers claiming to have represented Tenant and Landlord in connection with this Amendment.

h. Each signatory of this Amendment represents hereby that he or she has the authority to execute and deliver the same on behalf of the party hereto for which such signatory is acting.

[SIGNATURES ARE ON FOLLOWING PAGE]

IN WITNESS WHEREOF , Landlord and Tenant have duly executed this First Amendment of Lease as of the Amendment Effective Dat e as a document under seal .

LANDLORD:

ASTRAZENECA PHARMACEUTICALS LP , a Delaware limited partnership

By: _/s/ Kumar Srinivasan_____

Name: _Kumar Srinivasan_____

Title: _Vice President_____

TENANT:

CERULEAN PHARMA INC. , a Delaware corporation

By: _/s/ Christopher D. T. Guiffre_____

Name: _Christopher D. T. Guiffre_____

Title: _President & Chief Executive Officer_

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 Statements No. 333-211697 on Form S-8 and No. 333-206396 on Form S-3 of our report dated March 30, 2017, relating to the consolidated financial statements of Cerulean Pharma Inc. and subsidiary (which report expresses an unqualified opinion and includes an explanatory paragraph relating to the substantial doubt about the Company's ability to continue as a going concern) appearing in this Annual Report on Form 10-K of Cerulean Pharma Inc. for the year ended December 31, 2016.

/s/ DELOITTE & TOUCHE LLP

Boston, Massachusetts
March 31, 2017

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 31, 2017

/s/ Christopher D. T. Guiffre

Christopher D.T. Guiffre
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Gregg D. Beloff, 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 31, 2017

/s/ Gregg D. Beloff

Gregg D. Beloff
Interim Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Cerulean Pharma Inc. (the "Company") for the year ended December 31, 2016, 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 31, 2017

/s/ Christopher D. T. Guiffre

Christopher D.T. Guiffre
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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

In connection with the Annual Report on Form 10-K of Cerulean Pharma Inc. (the "Company") for the year ended December 31, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Gregg D. Beloff, Interim Chief Financial 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 31, 2017

/s/ Gregg D. Beloff
Gregg D. Beloff
Interim Chief Financial Officer
(Principal Financial Officer)