SPECTRUM PHARMACEUTICALS INC
Form 10-K
March 14, 2016
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

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x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2015

.. TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission File Number: 001-35006

SPECTRUM PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware (State or other jurisdiction of incorporation or organization)	93-0979187 (I.R.S. Employer Identification No.)
11500 South Eastern Avenue, Suite 240 Henderson, Nevada 89052 (Address of principal executive offices)	
(702) 835-6300 (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, $0.001 par value	The NASDAQ Stock Market, LLC
Rights to Purchase Series B Junior Participating Preferred Stock	

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x
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 x
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T

(§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 232.405 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 x

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 x
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 x

As of June 30, 2015, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant was $459,959,918 (based upon the $6.84 per share closing sale price for shares of the Registrant's Common Stock as reported by the NASDAQ Global Select Market on June 30, 2015, the last trading date of the Registrant's most recently completed second fiscal quarter).

As of February 29, 2016, approximately 68,163,483 shares of the Registrant's Common Stock, $0.001 par value, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for the registrant's 2016 Annual Meeting of Stockholders, to be filed on or before April 29, 2016, are incorporated by reference into Part III, Items 10-14 of this Annual Report on Form 10-K.

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Cautionary Note Concerning Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934 as amended (the "Exchange Act"), in reliance upon the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, without limitation, statements regarding our future product development activities and costs, the revenue potential (licensing, royalty and sales) of our products and product candidates, the success, safety and efficacy of our drug products, revenues, development timelines, product acquisitions, liquidity and capital resources and trends, and other statements containing forward-looking words, such as, "believes," "may," "could," "will," "expects," "intends," "estimates," "anticipates," "plans," "seeks," "continues," or the ne or variation thereon or similar terminology (although not all forward-looking statements contain these words). Such forward-looking statements are based on the reasonable beliefs of our management as well as assumptions made by and information currently available to our management. Readers should not put undue reliance on these forward-looking statements. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified; therefore, our actual results may differ materially from those described in any forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed elsewhere in this Annual Report on Form 10-K, and the following factors:

- our ability to successfully develop, obtain regulatory approval for and market our products;
- our ability to continue to grow sales revenue of our marketed products;
- risks associated with doing business internationally;
- our ability to generate and maintain sufficient cash resources to fund our business;
- our ability to enter into strategic alliances with partners for manufacturing, development and commercialization;
- efforts of our development partners;
- the ability of our manufacturing partners to meet our timelines;
- the ability to timely deliver product supplies to our customers;
- our ability to identify new product candidates and to successfully integrate those product candidates into our operations;
- the timing and/or results of pending or future clinical trials, and our reliance on contract research organizations;
- our ability to protect our intellectual property rights;
- competition in the marketplace for our drugs;
- delay in approval of our products or new indications for our products by the U.S. Food and Drug Administration, or the "FDA";
- actions by the FDA and other regulatory agencies, including international agencies;
- securing positive reimbursement for our products;
- the impact of any product liability, or other litigation to which we are, or may become a party;
- the impact of legislative or regulatory reform of the healthcare industry and the impact of recently enacted healthcare reform legislation;
- the availability and price of acceptable raw materials and components from third-party suppliers, and their ability to meet our demands;
- our ability, and that of our suppliers, development partners, and manufacturing partners, to comply with laws, regulations and standards, and the application and interpretation of those laws, regulations and standards, that govern or affect the pharmaceutical and biotechnology industries, the non-compliance with which may delay or prevent the development, manufacturing, regulatory approvals and sale of our products;
- defending against claims relating to improper handling, storage or disposal of hazardous chemical, radioactive or biological materials which could be time consuming and expensive;
- our ability to maintain the services of our key executives and technical and sales and marketing personnel;

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- the difficulty in predicting the timing or outcome of product development efforts and regulatory approvals; and
- demand and market acceptance for our approved products.

All subsequent written and oral forward-looking statements attributable to us or by persons acting on our behalf are expressly qualified in their entirety by these cautionary statements.

In addition, past financial or operating performance is not necessarily a reliable indicator of future performance, and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we do not undertake to update any such forward-looking statements and expressly disclaim any duty to update the information contained in this Annual Report on Form 10-K.

Unless the context otherwise requires, all references in this Annual Report on Form 10-K to the “Company”, “we,” “us,” “our,” “Spectrum” and “Spectrum Pharmaceuticals” refer to Spectrum Pharmaceuticals, Inc. and its subsidiaries and other consolidated entities, as a consolidated entity. We primarily conduct our business activities as Spectrum Pharmaceuticals.

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PART I

ITEM 1. BUSINESS

Company Overview and Business Strategy

Our primary strategy is comprised of acquiring, developing, and commercializing a broad and diverse pipeline of late-stage clinical and commercial products. In addition to an efficient in-house clinical development organization with regulatory and data management capabilities, we have established a commercial infrastructure for our marketed products. Currently, we have six approved oncology/hematology products that target different types of non-Hodgkin's lymphoma ("NHL"), advanced metastatic colorectal cancer, acute lymphoblastic leukemia ("ALL"), and multiple myeloma ("MM").

We also have two drugs in late stage development:

- SPI-2012, is being developed for chemotherapy-induced neutropenia in patients with breast cancer.
- EOQUIN® (previously referred to as APAZIQUONE for intravesical instillation), is being developed for immediate intravesical instillation post-transurethral resection of bladder tumors in patients with non-muscle invasive bladder cancer.

Our passion to identify, develop and deliver important options for patients suffering from cancer is behind every action we take. We are committed to excellence and strive to make a difference in the lives of patients every day.

Cancer Background and Market Size

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells, which can result in death. The development of cancer is multi-factorial and includes both external factors (tobacco, infectious organisms, chemicals, and radiation) and internal factors (inherited mutations, hormones, immune conditions, and mutations that occur from exposure to environmental factors or errors in making DNA (deoxyribonucleic acid) during normal cell division). These causal factors may act together or in sequence to initiate or promote the development of cancer. Ten or more years often pass between exposure to these factors and the development of detectable cancer. Cancer is treated through surgery, radiation, chemotherapy, hormone therapy, immune therapy, and/or targeted drug therapy.

According to the American Cancer Society’s publication Cancer Facts & Figures 2015, cancer is the second leading cause of death in the U.S. (only behind heart disease). In the U.S., approximately 1.7 million new cancer cases were

expected to be diagnosed in 2015 and over 589,000 persons were expected to die from the disease. Anyone can develop cancer. Since the

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risk of being diagnosed with cancer increases with age, most cases occur in adults who are middle aged or older. About 77% of all cancers are diagnosed in people 55 years of age and older. In the U.S., men have slightly less than a 1 in 2 lifetime risk of developing cancer; for women, the risk is a little more than 1 in 3. These probabilities are estimated based on the overall experience of the general population. Individuals within the population may have higher or lower risk because of differences in exposures (e.g., smoking), and/or genetic susceptibility. In addition, currently available treatments are variably effective in the different cancers and individual patients. Together these patients' risks and the treatment limitations suggest a significant current and long-term demand for improved and novel cancer treatments.

Product Portfolio

We have a product portfolio consisting of both commercial stage and development stage products that address various cancer types (see "Research & Development" section below for our pipeline of cancer therapeutics that are in various development stages). We remain committed to growing the sales of our currently marketed products, as we strive to maintain a robust development pipeline.

Commercialized Products

Our commercialized drug products (or pending commercial launch in the case of EVOMELA), and their approved indications, are summarized in the following table:

FUSILEV

FUSILEV (levoleucovorin), a novel folate analog and the pharmacologically active isomer (the levo-isomer) of the racemic compound, calcium leucovorin. Leucovorin is a mixture of equal part of both isomers: the pharmacologically active levo-isomer and the inactive dextro-isomer. Preclinical studies have demonstrated that the inactive dextro-isomer may compete with the active levo-isomer for uptake at the cellular level. By removing the inactive dextro form, the dosage of FUSILEV is one-half that of leucovorin and patients are spared the administration of an inactive substance. FUSILEV is approved as a ready-to-use solution, and as freeze-dried powder. FUSILEV has the following indications for use:

- in combination chemotherapy with 5-fluorouracil in the palliative treatment of patients with advanced metastatic colorectal cancer, or mCRC.
- for rescue after high-dose methotrexate therapy in osteosarcoma; and
- to diminish the toxicity and counteract the effects of impaired methotrexate elimination and of inadvertent over dosage of folic acid antagonists.

FOLOTYN

FOLOTYN (pralatrexate injection), a folate analogue metabolic inhibitor, was discovered by Memorial Sloan-Kettering Cancer Center, SRI International and Southern Research Institute and developed by Allos Therapeutics, Inc. ("Allos"). In September 2009, the FDA granted accelerated approval for FOLOTYN for use as a single agent for the treatment of patients

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with relapsed or refractory PTCL. FOLOTYN was the first chemotherapy approved by the FDA, under its accelerated approval program, for the treatment of relapsed or refractory PTCL and has been available to patients in the U.S. since October 2009.

According to the Lymphoma Research Foundation, lymphoma is the most common blood cancer. Hodgkin's lymphoma and non-Hodgkin's lymphoma ("NHL") are the two main forms of lymphoma. Lymphoma occurs when lymphocytes, a type of white blood cell, grow abnormally and accumulate in one or more lymph nodes or lymphoid tissues. The body has two main types of lymphocytes that can develop into lymphomas: B-lymphocytes (B-cells) and T-lymphocytes (T-cells). PTCL comprises a group of rare and aggressive NHLs that develop from mature T-cells. PTCL accounts for approximately 5 to 15% of all NHL cases in the U.S and Europe.

Based on preclinical studies, we believe that FOLOTYN selectively enters cells expressing reduced folate carrier ("RFC"), a protein that is frequently over expressed on cancer cells compared to normal cells. Once inside cancer cells, FOLOTYN is efficiently polyglutamylated, which makes it less susceptible to efflux-based drug resistance and leads to high intracellular drug retention compared to other antifolates. Inside the cell, FOLOTYN targets the inhibition of dihydrofolate reductase ("DHFR"), an enzyme critical in the folate pathway, thereby interfering with DNA and RNA synthesis and triggering cancer cell death.

We are exploring additional settings for FOLOTYN where methotrexate ("MTX"), a drug in the same category as FOLOTYN, has been successfully used for decades in the treatment of breast cancer, bladder cancer, and lung cancer. We plan to test FOLOTYN's benefits in these settings because FOLOTYN is designed to provide greater activity than MTX. In addition to its use alone as a single agent, we are evaluating FOLOTYN as part of different chemotherapy combinations.

ZEVALIN

ZEVALIN (ibritumomab tiuxetan) injection for intravenous use is a prescription medication that is part of a three step treatment regimen consisting of: two treatments of rituximab and one treatment of Yttrium-90 (Y-90) ZEVALIN. The National Cancer Institute ("NCI") estimated 72,000 new cases of NHL in the U.S. in 2015. Rituximab is used to reduce the number of B-cells in the blood and Y-90 ZEVALIN is then given to treat NHL. It is currently approved in the U.S. and more than 40 countries outside the U.S. including countries in Europe, Latin America and Asia for (i) treatment of patients with recurring, low-grade or follicular B-cell NHL, after other anticancer drugs are no longer working, and (ii) newly diagnosed follicular NHL following a response to initial anticancer therapy.

MARQIBO

MARQIBO is a novel, sphingomyelin/cholesterol liposome-encapsulated formulation of the FDA-approved anticancer drug vincristine. MARQIBO's approved indication is for the treatment of adult patients with ALL in second or greater relapse or whose disease has progressed following two or more lines of anti-leukemia therapy. In the U.S., approximately 6,000 patients per year are diagnosed with ALL, of which approximately 1,600 can be categorized as ALL in second or greater relapse.

MARQIBO is also currently being explored for the treatment of the broader ALL indication as well as in NHL in addition to its approved treatment for Philadelphia chromosome-negative ALL.

BELEODAQ

BELEODAQ (belinostat) is a histone deacytelase, ("HDAC") inhibitor for the treatment of patients with relapsed or refractory PTCL. This indication was FDA approved in July 2014 under its accelerated approval program, based on tumor response rate and duration of response. BELEODAQ's anticancer effect is thought to be mediated through multiple mechanisms of action, including the inhibition of cell proliferation, induction of apoptosis (programmed cell death), inhibition of angiogenesis, induction of differentiation, and the activity in tumors that had become resistant to anticancer agents such as the platinums, taxanes and topoisomerase II inhibitors.

BELEODAQ is differentiated from other HDAC inhibitors that selectively inhibit a single class of HDAC enzymes because it inhibits all three classes of the zinc-dependent HDAC enzymes (Class I, Class II and Class IV); this leads to different alterations in histone and non-histone protein acetylation that, in turn, could importantly influence chromatin accessibility, gene transcription, and activity in different cancer patients, including those who develop drug resistant

disease.

BELEODAQ has many attributes that separate it from other currently marketed HDACs, including efficacy when used alone and in combination, less toxicities (when compared to the reported rates of some adverse events with the other currently-

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marketed HDACs), including less bone marrow toxicity, and a lack of other severe side effects, such as mucositis, that may enable full dose combinations of this drug with several other cytotoxic agents.

EVOMELA (previously referred to as Captisol-Enabled® MELPHALAN)

EVOMELA is intended for use as a conditioning treatment prior to autologous stem cell transplant for patients with MM. MM is a cancer of plasma cells, a type of white blood cell present mainly in the bone marrow that produces antibodies. In MM, a group of plasma cells (myeloma cells) become cancerous and multiply, raising the number of plasma cells to a higher-than-normal level, which can crowd out normal blood cells and lead to abnormally high proteins in the blood or urine. The NCI estimated 27,000 new cases of MM in the U.S. in 2015, with the incidence of new cases increasing by approximately 1.6% per year. The current intravenous Melphalan market is approximately $100 million annually, with predominant use in stem cell transplants.

The EVOMELA formulation avoids the use of propylene glycol (“PG”), which is required as a co-solvent in the currently-available formulation of this product. PG has been reported to cause adverse renal and cardiac side-effects that limit the ability to deliver higher quantities of intended therapeutic compounds. The use of Captisol technology to reformulate EVOMELA is anticipated to allow for longer administration durations and slower infusion rates, potentially enabling clinicians to avoid reductions, and safely achieve a higher dose intensity for pre-transplant chemotherapy.

EVOMELA was granted Orphan Drug status by the FDA for use as a high-dose conditioning regimen prior to hematopoietic progenitor (stem) cell transplantation. In December 2014, we filed our new drug application (“NDA”) for EVOMELA with the FDA. On October 23, 2015, we received a Complete Response Letter (“CRL”) from the FDA for this NDA that did not identify any clinical deficiencies, and we subsequently resubmitted our NDA. On March 10, 2016, the FDA communicated its approval of our NDA for EVOMELA as a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation in patients with MM, and for the palliative treatment of patients with MM for whom oral therapy is not appropriate. We plan to commercially launch EVOMELA as soon as possible.

Product Pipeline

SPI-2012

SPI-2012 is being investigated for the treatment of chemotherapy-induced neutropenia. In January 2012, we entered into a co-development and commercialization agreement for worldwide rights, except for Korea, China, and Japan, with Hanmi Pharmaceutical Co., Ltd. ("Hanmi"), for SPI-2012 based on Hanmi’s proprietary LAPSCOVERY Technology. Chemotherapy can cause myelosuppression and unacceptably low levels of white blood cells, making patients prone to infections, hospitalizations, and interruption of additional chemotherapy treatments.

Granulocyte colony-stimulating factor, or GCSF, stimulates the production of white blood cells by the bone marrow. A recombinant form of GCSF is used in appropriate cancer patients to accelerate recovery from neutropenia after chemotherapy, allowing higher-intensity treatment regimens to be given at full-dose and on schedule. We believe the worldwide annual market opportunity for GCSF-related drugs is over $6 billion.

In September 2014, we announced our decision to advance SPI-2012 to Phase 3 trials due to positive Phase 2 results in our collaboration program with Hanmi, and began discussions with the FDA and the European Medicines Agency (“EMA”) to discuss our Phase 3 design. In December 2015, we reached agreement with the FDA regarding our Phase 3 SPA for SPI-2012. We have designated more than 100 sites for this clinical trial, and initiated this Phase 3 clinical study beginning in January 2016. This trial will evaluate the safety and efficacy of SPI-2012 as a treatment for chemotherapy-induced neutropenia in patients with breast cancer, and will serve as the basis for our Biologics License Application ("BLA") filing.

POZIOTINIB

POZIOTINIB is a novel, oral pan-HER inhibitor that irreversibly blocks signaling through the Epidermal Growth Factor Receptor (EGFR, HER) Family of tyrosine-kinase receptors, including HER1 (erbB1; EGFR), HER2 (erbB2), HER4 (erbB4), and HER receptor mutations. This, in turn, leads to the inhibition of the proliferation of tumor cells that over-express these receptors. Mutations or over-expression/amplification of EGFR family receptors have been associated with a number of different cancers, including non-small cell lung cancer ("NSCLC"), breast cancer, and

gastric cancer. POZIOTINIB has shown single agent activity in the treatment of various cancer types, including breast, gastric, colorectal and lung cancers. POZIOTINIB has shown promising early clinical activity in Phase 1 trials in patients who had failed multiple lines of treatment

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including the HER2-directed therapies, trastuzumab and lapatinib. POZIOTINIB is currently being investigated by Hanmi in several mid-stage trials in different solid tumor indications including EGFR-mutant NSCLC, gastric cancer, head and neck cancer and HER2 positive breast cancer.

In November 2015, we submitted an Investigational New Drug ("IND") application with the FDA. In March 2016 we initiated our Phase 2 Breast Cancer Trial. The Phase 2 study is an open-label study that will enroll approximately 70 patients with HER-2 positive metastatic breast cancer, who have failed at least two HER-2 directed therapies. The dose and schedule of oral POZIOTINIB will be based on clinical experience from the studies in Korea, and in addition include the use of prophylactic therapies to help minimize known side-effects of HER-2 directed therapies.

In February 2015, we executed a global in-license agreement (excluding Korea and China) with Hanmi Pharmaceutical Co., Ltd for POZIOTINIB, a pan-HER inhibitor in Phase 2 clinical trials in return for our upfront payment and future regulatory and sales-dependent milestone payments. POZIOTINIB has shown single agent activity in the treatment of various cancer types, including breast, gastric, colorectal and lung cancers. In the Phase 1 study for this drug, 6 of 10 breast cancer patients demonstrated partial responses; we also believe the safety profile was consistent with similar drug classes, with four patients having a grade 3 diarrhea response.

EOQUIN (previously referred to as APAZIQUONE)

EOQUIN is a bio-reductive alkylating indoloquinone that is enzymatically activated by enzymes that are over expressed by bladder tumors that is being tested in non-muscle invasive bladder ("NMIBC").

The NCI estimates that the 2015 incidence and prevalence of bladder cancer in the U.S. was approximately 74,000 cases. The global presence of bladder cancer is estimated at 2.7 million cases. According to Botteman et al., (PharmacoEconomics 2003), bladder cancer is the most expensive cancer to treat on a lifetime basis. The overall cost of bladder cancer treatment in the U.S. is approximately $3.4 billion annually, most of which is related to the direct treatment of this disease.

The initial treatment of bladder cancer is to attempt a complete surgical removal of the tumor. However, bladder cancer is a highly recurrent disease with approximately 80% of patients recurring within five years, and a majority of patients recurring within two years. This high recurrence rate is attributed to:

- the highly implantable nature of cancer cells that are dispersed during surgery;
- incomplete tumor resection; and
- tumors present in multiple locations in the bladder which may be missed or too small to visualize at the time of resection.

Despite evidence in the published literature and guidance from the American and European Urology Associations, instillation of a chemotherapeutic agent immediately following surgery is not a standard clinical practice. Currently, there are no FDA approved drugs for this indication which may, in part, explain the difference between the literature and urology guidelines and actual clinical management of this disease. For more than 30 years, no new drugs have been introduced in the market for treatment of NMIBC. EOQUIN represents much needed therapy for patients and may provide a meaningful opportunity to reduce overall medical costs.

Pharmacokinetic studies have verified that EOQUIN is rarely detectable in the bloodstream of patients when it is administered either after surgical resection or as a part of a delayed multi-instillation protocol. EOQUIN is inactivated in the systemic circulation by the red blood cell fraction. The proposed dose therefore carries a minimal risk of systemic toxicity that could arise from absorption of a drug through the bladder wall into the bloodstream. These features of EOQUIN are distinct from other intravesical agents currently in use for the treatment of recurrent bladder cancer. An immediate instillation of EOQUIN may help by:

- reducing tumor recurrence by destroying dispersed cancer cells that would otherwise re-implant onto the inner lining of the bladder;
- destroying remaining cancer cells at the site of tumor resection (also known as chemo-resection); and
- destroying tumors not observed during resection (also known as chemo-ablation).

In August 2015, we reached agreement with the FDA on the Special Protocol Assessment ("SPA") of the planned Phase 3 clinical trial of EOQUIN. This trial commenced with its first patient dosing in October 2015, and is designed to evaluate the intravesical use of this drug for the treatment of patients with NMIBC as one or two instillations, immediately following

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transurethral resection of bladder tumor ("TURBT"). In December 2015, we submitted our NDA for EOQUIN with the FDA, based on the pooled results of a previous Phase 3 program. In February 2016, the FDA accepted the EOQUIN NDA for review and indicated that it plans to hold an advisory committee meeting regarding the NDA and set a target decision date of December 11, 2016.

Manufacturing

We currently do not have internal manufacturing capabilities; therefore, all of our products are manufactured on a contract basis. We expect to continue to contract with third-party providers for manufacturing and packaging services, including active pharmaceutical ingredients (“API”) and finished-dosage products. We believe that our current agreements with third-party manufacturers provide for sufficient operating capacity to support the anticipated commercial demand and clinical requirements for our products. However, we are actively seeking multiple supplier sources for all our drug products in order to mitigate the risk of over-reliance on any one supplier. We attempt to prevent supply disruption through supply agreements, appropriate forecasting, and maintaining base stock levels. We believe that we could quickly enter into another supply or manufacturing agreement on substantially similar terms if we were required to do so.

Sales and Marketing

We presently market and sell our pharmaceutical products through a direct sales force in the U.S., and through distributors in Europe (and previously in Japan). Our U.S. sales team is divided between “corporate accounts” and “oncology accounts.” The primary decision makers for our products are oncologists and hematologists. As of December 31, 2015, our U.S. sales force (management, representatives, and direct support) numbered 100 employees.

Customers

Our product sales are concentrated to large pharmaceutical distributors (that ship and bill to hospitals and clinics). The customers that represent 10% or more of our total gross product sales in 2015, 2014 and 2013 are as follows:

	Product Sales		
	2015	2014	2013
Oncology Supply, a division of ASD Specialty Healthcare, Inc., and its affiliates (excluding ICS)	36.7 %	40.4 %	35.4 %
McKesson Corporation and its affiliates	34.2 %	32.9 %	19.8 %
Cardinal Health, Inc. and its affiliates	17.4 %	*	*
Integrated Commercialization Solutions, Inc. (“ICS”)	*	*	15.8 %

* Less than 10%

We are exposed to credit risk associated with trade receivables that result from these product sales. We do not require collateral or deposits from our customers due to our assessment of their creditworthiness and our long-standing relationship with them. We maintain reserves for potential bad debt, though credit losses have historically been nominal and within management’s expectations. A summary of our customers that represent 10% or more of our accounts receivables, net, as of December 31, 2015 and 2014 are as follows:

	Accounts Receivable, net	
	December 31, 2015	December 31, 2014
McKesson Corporation and its affiliates	66.7 %	31.9 %
Cardinal Health, Inc. and its affiliates	23.8 %	*
Oncology Supply, a division of ASD Specialty Healthcare, Inc., and its affiliates (excluding ICS)	*	51.1 %
ICS	*	11.9 %

* Less than 10%

Competition

The pharmaceutical industry is characterized by rapidly-evolving biotechnology and intense competition, which we expect will continue. Many companies are engaged in research and development of compounds that are similar to ours – both commercialized and in development. In the event that one or more of our competitor's programs are successful, the market for

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some of our drug products could be reduced or eliminated. Any product for which we obtain FDA approval must also compete for market acceptance and market share.

Successful marketing of branded products depends primarily on the ability to communicate the effectiveness, safety, and value of the products to healthcare professionals in private practice, group practices, hospitals, academic institutions and managed care organizations. Competition for branded drugs is less driven by price and is more focused on innovation in treatment of disease, advanced drug delivery, and specific clinical benefits over competitive drug therapies. Unless our products are shown to be differentiated, i.e., have a better safety profile, efficacy, and cost-effectiveness, as compared to other alternatives, they may not gain acceptance by medical professionals and may therefore never be commercially successful.

Companies that have products on the market or in research and development that target the same indications as our products include, among others, Astra Zeneca PLC, Bayer AG, Endo International plc, Eli Lilly and Co., Novartis AG, Genentech, Inc. (Roche), Bristol-Myers Squibb Company, GlaxoSmithKline, Biogen-IDEC Pharmaceuticals, Inc., OSI Pharmaceuticals, Inc. (Astellas Pharma), Cephalon, Inc. (Teva Pharmaceuticals), Sanofi-Aventis, Inc., Pfizer, Inc., Genta Incorporated, Merck, Celgene Corporation, BiPar Sciences, Inc., Genzyme Corporation, Shire Pharmaceuticals, AbbVie, Poniard Pharmaceuticals, Inc., and Johnson & Johnson.

Each of the aforementioned companies may be more advanced in development of competing drug products. Many of these competitors are large and well-capitalized companies focusing on a wide range of cancers and drug indications, and have substantially greater resources and expertise than we do.

We believe that the current competitive landscape for each of our commercialized products is as follows:

(a) FUSILEV is the levo-isomeric form of the racemic compound calcium, leucovorin, a product already approved for the same indication as FUSILEV. As there are currently two generic companies approved by the FDA to sell the leucovorin product, we are competing with a lower-cost alternative. In addition, as discussed in Section 1A, Risks Related to Our Business, FUSILEV faces competition from generic levo-leucovorin.

(b) ZEVALIN has two competitive products for its currently approved indications:

- Rituxan® (rituximab), marketed by Genentech and Biogen-IDEC Pharmaceuticals, is indicated for the treatment of patients with relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent; previously untreated follicular, CD20-positive, B-cell NHL in combination with CVP (cyclophosphamide, vincristine and prednisone combination) chemotherapy; and non-progressing (including stable disease), low-grade, CD20-positive B-cell NHL, as a single agent, after first-line CVP chemotherapy. Rituxan is administered as a part of various chemotherapy regimens and schedules, the vast majority of which, could be used in concert with other therapeutic agents, such as ZEVALIN, as part of a treatment plan.

- Treanda® (bendamustine hydrochloride) for Injection, for Intravenous Infusion, marketed by Cephalon, is indicated for the treatment of patients with indolent B-cell NHL that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

(c) FOLOTYN, the first agent approved by the FDA for treatment of patients with relapsed or refractory PTCL, has two competitive products for its currently approved indications:

- Romidepsin, marketed by Celgene, Inc., was granted accelerated approval by the FDA in June 2011 for the treatment of patients with PTCL who have received at least one prior therapy. This was the second indication approved for romidepsin, which was initially approved by the FDA in November 2009 for the treatment of patients with CTCL who have received at least one prior systemic therapy.

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Brentuximab vedotin, marketed by Seattle Genetics, Inc., was also granted accelerated approval by the FDA in August 2011 for two indications, one of which was for the treatment of patients with systemic anaplastic large cell lymphoma ("ALCL") after failure of at least one prior multi-agent chemotherapy regimen. ALCL is one of the subtypes of PTCL included in the labels of both FOLOTYN and romidepsin.

We are aware of multiple investigational agents that are currently being studied in clinical trials for PTCL, including alisertib, which, if approved, may compete with FOLOTYN in the U.S. Because of the natural history of PTCL with repeated treatment failures, it is likely that many patients would receive treatment with more than one agent (e.g., BELEODAQ and

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FOLOTYN). In addition, there are many existing approaches used in the treatment of relapsed or refractory PTCL, including combination chemotherapy and single agent regimens, which represent competition for FOLOTYN.

(d) MARQIBO is a next generation liposomal form of standard vincristine. In its current indication, MARQIBO is approved for adult patients with relapsed or refractory Ph-ALL who have not responded or relapsed after two prior treatments. Currently, standard vincristine is not approved for the same indication as MARQIBO.

(e) BELEODAQ is a histone deacetylase inhibitor indicated for the treatment of patients with relapsed or refractory PTCL. This indication is approved under accelerated approval based on tumor response rate and duration of response. An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.

Research and Development

New drug development is the process whereby drug product candidates are tested for the purpose of filing a BLA in the U.S. (or similar filing in other countries). Obtaining marketing approval from the FDA or similar regulatory authorities outside of the U.S. is an inherently uncertain, lengthy and expensive process that requires several phases of clinical trials to demonstrate to the satisfaction of the appropriate regulatory authorities that the products are both safe and effective for their respective indications. Our development focus is primarily based on acquiring and developing late-stage development drugs as compared to new drug discovery, which is particularly uncertain and lengthy.

Our in-development products are summarized below:

Our research and development expenses for drug development are comprised of our personnel expenses, contracted services with third parties, license fees and milestone payments to third parties, clinical trial costs, laboratory supplies, drug products, and certain allocations of corporate costs. The below table summarizes our research and development expenses by project in 2015, 2014 and 2013:

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	Research and Development Expenses for the Year Ended December 31, (in thousands)		
	2015	2014	2013
EOQUIN (previously APAZIQUONE)	$ 4,147	$ 1,377	$ 1,078
BELEODAQ	1,320	20,911 *	6,733
FUSILEV	885	442	4,517
FOLOTYN	2,650	4,927	2,992
ZEVALIN	3,025	6,950	8,572
SPI-2012	1,133	4,141	1,403
MARQIBO	4,412	6,623	4,099
EVOMELA (previously CE-MELPHALAN)	8,568	5,966	3,400
POZIOTINIB	4,240	—	—
Other in-development compounds and drugs	633	1,967	3,632
Total — Direct costs	31,013	53,304	36,426
Add: General research and development expenses (including personnel costs that correspond to more than one in-development project)	21,571	21,073	13,335
(Less): Reimbursements from development partners for SPI-2012 and BELEODAQ	(521)	(2,758)	(804)
(Less): Incurred FOLOTYN study costs that reduce our drug development liability (see Note 16)	(1,297)	(1,957)	(2,287)
Total research and development expenses	$ 50,766	$ 69,662	$ 46,670

* Inclusive of 2014 milestone payment of $17.8 million.

Patents and Proprietary Rights

Our Patents and Proprietary Rights

We in-license from third parties certain patent and related intellectual property rights related to our proprietary drug products. Under most of these license arrangements, we are generally responsible for all development, patent filing and maintenance costs, sales, marketing and liability insurance costs related to the drug products.

In addition, these licenses and agreements may require us to make royalty and other payments and to reasonably utilize the underlying technology of applicable patents. If we fail to comply with these and other terms in these licenses and agreements, we could lose the underlying rights to one or more of our potential products, which would adversely affect our product development and harm our business.

The protection, preservation and infringement-free commercial utilization of these patents and related intellectual property rights are very important to the successful execution of our strategy. However, the issuance of a patent is neither conclusive as to its validity nor as to the enforceable scope of the claims of the patent. Accordingly, our patents and the patents we have licensed may not prevent other companies from developing similar or functionally equivalent products or from successfully challenging the validity of our patents. If our patent applications are not allowed or, even if allowed and issued as patents, if such patents or the patents we have in-licensed are circumvented or not upheld by the courts, our ability to competitively utilize our patented products and technologies may be significantly reduced. Also, such patents may or may not provide competitive advantages for their respective products or they may be challenged or circumvented by competitors, in which case our ability to commercially sell these products may be diminished.

From time-to-time, we may need to obtain licenses to patents and other proprietary rights held by third parties to develop, manufacture and market our products. If we are unable to timely obtain these licenses on commercially reasonable terms, our ability to commercially exploit such products may be inhibited or prevented.

We believe that our patents and licenses are critical to operating our business, as summarized below by commercialized and in-development drug products.

FUSILEV: Fusilev had/has orphan drug exclusivity for two indications. These indications are for the treatment of (i) osteosarcoma (which expired on March 7, 2015) and (ii) metastatic colorectal cancer (which expires on April 29, 2018). FUSILEV also had/has a U.S. composition of matter patent that expires in March 2022.

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In February 2015, the U.S. District Court for the District of Nevada found the asserted claims of the patent covering FUSILEV to be invalid, and on October 2, 2015, the Court of Appeals for the Federal Circuit affirmed that decision. On April 27, 2015, we filed suit in the U.S. District Court for the District of Columbia against the FDA seeking a temporary restraining order or preliminary injunction to suspend FDA approval of Sandoz Inc.'s ("Sandoz") Abbreviated New Drug Application ("ANDA"). The Company contends that Sandoz's ANDA should not have been approved until the expiry of our Orphan Drug Exclusivity on April 29, 2018. On April 29, 2015, the court denied the temporary restraining order and on May 27, 2015, the court entered summary judgment in favor of the FDA et al. On June 5, 2015, we filed our Notice of Appeal. Oral argument was held October 22, 2015. The ultimate outcome of this proceeding is uncertain.

ZEVALIN: We have sublicensed U.S. patents that cover the processes and tools for making monoclonal anti-bodies or MABs, in general, licensed U.S. patents that cover the CD-20 MAB in ZEVALIN as well as the use of ZEVALIN to treat NHL, and acquired patents covering the ZEVALIN compounding process (i.e., process of linking the CD-20 MAB to a radioactive isotope to make the patient-ready dosage form of ZEVALIN). These patents expire over a wide range of dates, and the licensed patents covering the CD-20 MAB began to expire in 2015. Additionally, we have U.S. patents covering the compounding process expiring in 2019, and we are considering filing new patent applications.

FOLOTYN: We have a composition of matter patent due to expire in 2022 following a five-year patent term extension in U.S. The composition of matter patent is due to expire in Europe in 2017 but is eligible for a similar patent term extension following regulatory approval in Europe. We also have patents covering the use of FOLOTYN for PTCL that will not expire until 2025. Additionally, we are considering filing new patent applications.

MARQIBO: We have U.S. and European patents covering the use of MARQIBO for leukemia, lymphoma and melanoma, and a U.S. patent covering the MARQIBO kit, all expiring in 2020. We have filed a patent cooperation treaty ("PCT") application claiming a method of encapsulating vincristine sulphate into liposomes. We are presently in the process of developing a “single vial” formulation of MARQIBO, and if we are successful, we believe our U.S. patent coverage could be extended to 2036.

BELEODAQ: The composition of matter patents that cover BELEODAQ and related compounds do not begin to expire until 2027. Currently, there are multiple U.S. and foreign patent applications pending that cover BELEODAQ formulations, uses and manufacturing and synthesis processes. We plan to file additional U.S. and foreign patent applications covering new formulations, uses, and manufacturing and synthesis processes.

EOQUIN: The U.S. formulation patent does not expire until 2022, and method of treatment of bladder cancer using a stabilized formulation that does not expire until 2024. Formulation patents outside the U.S. are due to expire in 2022. We have filed and plan to file additional U.S. and foreign patent applications covering new formulations and/or uses for this product.

SPI-2012: Composition of matter patents covering SPI-2012 are due to expire in 2025 in the U.S. and in 2024 outside the U.S. SPI-2012 is also covered by additional patents claiming various aspects of the technology that are due to expire between 2024 and 2030 and have filed patent applications for its formulation.

EVOMELA: This drug is covered by issued patents claiming improved Captisol ® technology that are due to expire between 2025 and 2029 in the U.S. Outside the U.S., we have issued patents that cover improved Captisol technology that are due to expire in 2025 and pending applications with anticipated expiry in 2029, if issued. We also have filed patent application covering Captisol-based formulation of EVOMELA in the U.S. and a number of other countries.

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We are constantly evaluating our patent portfolio and are currently assessing and filing patent applications for our drug products and are considering new patent applications in order to maximize the life cycle of each of our products. While the U.S. and the European Union (the "EU") are currently the largest potential markets for most of our products, we also have patents issued and patent applications pending outside of the U.S. and Europe. Limitations on patent protection in these countries, and the differences in what constitutes patentable subject matter in countries outside the U.S., may limit the protection we have on patents issued or licensed to us outside of the U.S. In addition, laws of foreign countries may not protect our intellectual property to the same extent as would laws in the U.S.

To minimize our costs and expenses and to maintain effective protection, we usually focus our patent and licensing activities within the U.S., the EU, Canada and Japan. In determining whether or not to seek a patent or to license any patent in a certain foreign country, we weigh the relevant costs and benefits, and consider, among other things, the market potential and profitability, the scope of patent protection afforded by the law of the jurisdiction and its enforceability, and the nature of terms

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with any potential licensees. Failure to obtain adequate patent protection for our proprietary drugs and technology would impair our ability to be commercially competitive in these markets.

In conducting our business, we rely upon trade secrets, know-how, and licensing arrangements. We use customary practices for the protection of our confidential and proprietary information such as confidentiality agreements and trade secret protection measures. It is possible that these agreements will be breached or will not be enforceable in every instance, and that we will not have adequate remedies for any such breach. It is also possible that our trade secrets or know-how will otherwise become known or independently developed by competitors. The protection of know-how is particularly important because it is often necessary or useful information that allows us to practice the claims in the patents related to our proprietary drug products.

In addition to the specific intellectual property subjects discussed above, we have trademark protection in the U.S. for Spectrum Pharmaceuticals, Inc.®, FUSILEV®, MARQIBO®, BELEODAQ®, EOQUIN®, Spectrum Therapy Access Resources, STAR, ZEVALIN®, FOLOTYN flower design associated with FOLOTYN and RenaZorb®. We also have the FOLOTYN trademark and the associated flower design registered in Europe and other countries. Additionally, we have pending U.S. and ex-U.S. trademark applications for other potential marks.

The Patent Process

The U.S. Constitution provides Congress with the authority to provide inventors the exclusive right to their discoveries. Congress codified this right in U.S. Code Title 35, which gave the United States Patent and Trademark Office ("USPTO") the right to grant patents to inventors and defined the process for securing a U.S. patent. This process involves the filing of a patent application that instructs a person having ordinary skill in the respective art how to make and use the invention in clear and concise terms. The invention must be novel (i.e., not previously known) and non-obvious (i.e., not an obvious extension of what is already known). The patent application concludes with a series of claims that specifically describe the subject matter that the patent applicant considers his invention.

The USPTO undertakes an examination process that can take from one to seven years, or more, depending on the complexity of the patent and the problems encountered during examination.

In exchange for disclosing the invention to the public, for all U.S. patent applications filed after 1995, the successful patent applicant is currently provided a right to exclude others from making, using or selling the claimed invention for a period of 20 years from the effective filing date of the patent application.

Under certain circumstances, a patent term may be extended. Patent extensions are most frequently granted in the pharmaceutical and medical device industries under the Drug Price Competition and Pricing Term Restoration Act of 1984, or the Hatch-Waxman Act, to recover some of the time lost during the FDA regulatory process, subject to a number of limitations and exceptions. The patent term may be extended up to a maximum of five years; however, as a general rule, the average extension period granted for a new drug is approximately three years. Only one patent can be extended per FDA approved product, and a patent can only be extended once.

Product Exclusivity

Under the Hatch-Waxman Act, drug products are provided exclusivity whereby the FDA will not accept applications to market a generic form of an innovator reference listed drug product until the end of the prescribed period. A product is granted a five-year period of exclusivity if it contains a chemical entity never previously approved by the FDA either alone or in combination, although generic applications may be submitted after four years if they contain a certification of patent invalidity or non-infringement as further discussed below. A three-year period of exclusivity is granted to a previously approved product based on certain changes (e.g., in strength, dosage form, route of administration or conditions of use), where the application is supported by new clinical investigations that are essential to approval. In addition, in 1997, Congress amended the law to provide an additional six months of exclusivity as a reward for studying drugs in children. This pediatric exclusivity, which can be obtained during the approval process or after approval, effectively delays the approval of a generic application until six months after the expiration of any patent or other exclusivity that would otherwise delay approval, thus providing an additional six months free of generic competition. In order to qualify for pediatric exclusivity, the FDA must make a written request for pediatric studies, the application holder must agree to the request and complete the studies within the required

timeframe, and the studies must be accepted by the FDA based on a determination that the studies fairly respond to the request. The provisions were enacted with a five-year sunset date, and have been reauthorized in 2002, 2007 and 2012.
Generic Approval and Patent Certification

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The Hatch-Waxman Act also created the ANDA, approval process, which permits the approval of a generic version of a previously approved branded drug without the submission of a full NDA, and based in part on the FDA's finding of safety and effectiveness for the reference listed drug. Applicants submitting an NDA are required to list patents associated with the drug product, which are published in the FDA Orange Book, and the timing of an ANDA approval depends in part on patent protection for the branded drug. When an ANDA is filed, the applicant must file a certification for each of the listed patents for the branded drug, stating one of the following: (1) that there is no patent information listed; (2) that such patent has expired; (3) that the patent will expire on a particular date (indicating that the ANDA may be approved on that date); or (4) that the drug for which approval is sought either does not infringe the patent or the patent is invalid, otherwise known as paragraph IV certification. If an ANDA applicant files a paragraph IV certification, it is required to provide the patent holder with notice of that certification. If the patent holder brings suit against the ANDA applicant for patent infringement within 45 days of receiving notice, the FDA may not approve the ANDA until the earlier of (i) 30 months from the patent holder's receipt of the notice (the 30-month stay) or (ii) the issuance of a final, non-appealed, or non-appealable court decision finding the patent invalid, unenforceable or not infringed.

The Hatch-Waxman Act also provided an incentive for generic manufacturers to file paragraph IV certifications challenging patents that may be invalid, unenforceable, or not infringed, whereby the first company to successfully challenge a listed patent and receive ANDA approval is protected from competition from subsequent generic versions of the same drug product for up to 180 days after the earlier of (1) the date of the first commercial marketing of the first-filed ANDA applicant's generic drug or (2) the date of a decision of a court in an action holding the relevant patent invalid, unenforceable, or not infringed. These 180-day exclusivity provisions have been the subject of litigation and administrative review, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, amended the provisions in several ways, including by providing that an ANDA applicant entitled to 180-day exclusivity may lose such exclusivity if any of the following events occur: (1) failure to market; (2) withdrawal of the ANDA; (3) change in patent certification; (4) failure to obtain tentative approval; (5) illegal settlement agreement; and (6) patent expiration.

With respect to the illegal settlement prong, the MMA amendments require that certain types of settlement agreements entered into between branded and generic pharmaceutical companies related to the manufacture, marketing and sale of generic versions of branded drugs are required to be filed with the Federal Trade Commission and the Department of Justice for review of potential anti-competitive practices. This requirement could affect the manner in which generic drug manufacturers resolve intellectual property litigation and other disputes with branded pharmaceutical companies, and could result generally in an increase in private-party litigation against pharmaceutical companies. The impact of this requirement, and the potential governmental investigations and private-party lawsuits associated with arrangements between brand name and generic drug manufacturers, remains uncertain. In addition, Congress has considered enacting legislation that would prohibit such settlements between brand name and generic drug manufacturers. Such a provision was considered as part of the Patient Protection and Affordable Care Act, or PPACA, signed into law on March 23, 2010. However, Congress removed the provision prior to passage. It is possible that Congress will again consider a ban on such settlements between brand name and generic drug manufacturers in the future.

The PPACA provides exclusivity protections for certain innovator biological products and a framework for FDA review and approval of biosimilar and interchangeable versions of innovator biologic products. The PPACA provides that no application for a biosimilar product may be approved until 12 years after the date on which the innovator product was first licensed, and no application may be submitted until four years after the date of first licensure. Products deemed interchangeable (as opposed to biosimilar) are also eligible for certain exclusivity.

Orphan Drug Designation

Some jurisdictions, including Europe and the U.S., may designate drugs for relatively small patient populations as "orphan" drugs. The FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., and a drug may also be considered an orphan even if the drug treats

a disease or condition affecting more than 200,000 individuals in the U.S. Orphan drug designation does not necessarily convey any advantage in, or shorten the duration of, the regulatory review and process for marketing approval. If a product with an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to seven years of orphan drug exclusivity, during which time the FDA will not approve any other application to market the same drug for the same indication except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Also, competitors are not prohibited from receiving approval to market the same drug or biologic for a different indication than that which received orphan approval.

Under EU medicines laws, the criteria for designating an “orphan medicinal product” are similar in principle to those in the U.S. Criteria for orphan designation are set out in Article 3 of Regulation (EC) 141/2000 on the basis of two alternative

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conditions. A medicinal product may be designated as orphan if it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU, when the application is made. This is commonly known as the “disease prevalence criterion” Alternatively, a product may be so designated if it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the EU and if without incentives it is unlikely that the marketing of the product in the EU would generate sufficient return to justify the necessary investment. This is commonly known as the “insufficient return criterion.”

These two alternative criteria must cumulatively meet the second condition that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. “Significant benefit” is defined in Regulation (EC) 847/2000 as a clinically relevant advantage or a major contribution to patient care.

Upon grant of a marketing authorization, orphan medicinal products are entitled to ten years of market exclusivity in respect of the approved therapeutic indication. Within the period of market exclusivity, no competent authority in the EU is permitted to accept an application for marketing authorization, a variation or a line-extension for the same approved therapeutic indication in respect of a similar medicinal product pursuant to Article 8.1 of Regulation 141/2000 unless one of the derogations set out in Article 8.3 of the same Regulation applies. In order to determine whether two products are considered similar, Regulation 847/2000 requires an assessment of the principal molecular structure and the underlying mode of action. Any minor variation or modification of the principal molecular structure would not ordinarily render the second product dissimilar to the first authorized product.

In order for the second applicant to break the market exclusivity granted to the first authorized similar medicinal product in respect of the same therapeutic indication, the second applicant would principally rely upon data to demonstrate that its product is safer, more efficacious or clinically superior to the first product pursuant to Article 8.3I of Regulation 141/2000. Ordinarily, such an assessment will require a head-to-head comparative clinical trial for the purpose of demonstrating clinical superiority.

The 10-year market exclusivity may be reduced to six years if at the end of the fifth year it is established that the product no longer meets the criteria for orphan designation on the basis of available evidence. To date, each of our five commercialized drugs continues to meet the orphan drug designation requirements.

FUSILEV had/has been granted orphan drug designations for its use in conjunction with high dose methotrexate in the treatment of osteosarcoma and for its use in combination chemotherapy with the approved agent 5-fluorouracil in the palliative treatment of metastatic adenocarcinoma of the colon and rectum (colorectal cancer). In addition, FOLOTYN has been granted an orphan drug designation for the treatment of T-cell lymphoma and BELEODAQ has been granted an orphan drug designation for PTCL. Lastly, MARQIBO has been granted orphan drug designations for its use in the treatment of adult patients with ALL in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies, and ZEVALIN has orphan drug designations for the treatment of patients with relapsed or refractory low-grade, follicular, or transformed B-cell NHL, including patients with Rituximab refractory follicular NHL.

Governmental Regulation

The development, production and marketing of our proprietary and generic drug and biologic products are subject to regulation for safety, efficacy and quality by numerous governmental authorities in the U.S. and other countries. In the U.S., drugs and biologics are subject to rigorous regulation. The Federal Food, Drug, and Cosmetic Act, as amended from time to time, and the regulations promulgated there under, as well as other federal and state statutes and regulations, govern, among other things, the development, approval, manufacture, safety, labeling, storage, record keeping, distribution, promotion, and advertising of our products. Product development and approval within this regulatory framework, including for drugs already at a clinical stage of development, can take many years and require the expenditure of substantial resources, and to obtain FDA approval, a product must satisfy mandatory quality, safety and efficacy requirements. In addition, each drug-manufacturing establishment must be registered with the FDA. Domestic manufacturing establishments must comply with the FDA’s current Good Manufacturing Practices (“cGMP”),

regulations and are subject to inspections by the FDA. To supply drug ingredients or products for use in the U.S., foreign manufacturing establishments must also comply with cGMP and are subject to inspections by the FDA or by other regulatory authorities in certain countries under reciprocal agreements with the FDA.

General Information about the Drug Approval Process and Post-Marketing Requirements

The U.S. system of new drug and biologics approval is a rigorous process. Only a small percentage of compounds that enter the pre-clinical testing stage are ever approved for commercialization. Our strategy focuses on in-licensing clinical stage

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drug products that are already in or about to enter human clinical trials. A late-stage focus helps us to effectively manage the high cost of drug development by focusing on compounds that have already passed the many hurdles in the pre-clinical and early clinical process.

The following general comments about the drug approval process are relevant to the development activities we are undertaking with our proprietary products.

Pre-clinical Testing: During the pre-clinical testing stage, laboratory and animal studies are conducted to show biological activity of a drug or biologic compound against the targeted disease. The compound is evaluated for safety. While all of our compounds are currently in clinical trials, it is possible that additional pre-clinical testing could be requested by a regulatory authority for any of our compounds.

Investigational New Drug Application: After certain pre-clinical studies are completed, an Investigational New Drug ("IND") application is submitted to the FDA to request the ability to begin human testing of the drug or biologic. An IND becomes effective thirty days after the FDA receives the application (unless the FDA notifies the sponsor of a clinical hold), or upon prior notification by the FDA.

Phase 1 Clinical Trials: These trials typically involve small numbers of healthy volunteers or patients and usually define a drug candidate's safety profile, including the safe dosage range.

Phase 2 Clinical Trials: In Phase 2 clinical trials, controlled studies of human patients with the targeted disease are conducted to assess the drug's effectiveness. These studies are designed primarily to determine the appropriate dose levels, dose schedules and route(s) of administration, and to evaluate the effectiveness of the drug or biologic on humans, as well as to determine if there are any side effects on humans to expand the safety profile following Phase 1. These clinical trials, and Phase 3 trials discussed below, are designed to evaluate the product's overall benefit-risk profile, and to provide information for physician labeling.

Phase 3 Clinical Trials: This phase usually involves a larger number of patients with the targeted disease. Investigators (typically physicians) monitor the patients to determine the drug candidate's efficacy and to observe and report any adverse reactions that may result from long-term use of the drug on a large, more widespread, patient population. During the Phase 3 clinical trials, typically the drug candidate is compared to either a placebo or a standard treatment for the target disease.

New Drug Application or Biologic License Application: After completion of all three clinical trial Phases, if the data indicates that the drug is safe and effective, a NDA or BLA is filed with the FDA requesting FDA approval to market the new drug as a treatment for the target disease.

Fast Track and Priority Review: The FDA has established procedures for accelerating the approval of drugs to be marketed for serious or life threatening diseases for which the manufacturer can demonstrate the potential to address unmet medical needs.

Abbreviated New Drug Application: An ANDA is an abbreviated new drug application for generic drugs created by the Hatch-Waxman Act. When a company files an ANDA, it must make a patent certification regarding the patents covering the branded product listed in the FDA's Orange Book. The ANDA drug development process generally takes less time than the NDA drug development process since the ANDA process usually does not require new clinical trials establishing the safety and efficacy of the drug product.

NDA/BLA and ANDA Approval: The FDA approves drugs and biologics that are subject to NDA and BLA review based on data in the application demonstrating the product is safe and effective in its proposed use(s) and that the product's benefits outweigh its risks. The FDA will also review the NDA or BLA applicant's manufacturing process and controls to ensure they are adequate to preserve the drug's identity, strength, quality, and purity. Finally, the FDA will review and approve the product's proposed labeling. As for the ANDA approval process, these "abbreviated" applications are generally not required to include preclinical or clinical data to establish safety and effectiveness. Rather, an ANDA must demonstrate both chemical equivalence and bio-equivalence (the rate and extent of absorption in the body) to the innovator drug — unless a bio-equivalence waiver is granted by the FDA.

Phase 4 Clinical Trials: After a drug has been approved by the FDA, Phase 4 studies may be conducted to explore additional patient populations, compare the drug to a competitor, or to further study the risks, benefits and optimal use

of a drug. These studies may be a requirement as a condition of the initial approval of the NDA or BLA.

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Post-Approval Studies Requirements under FDAAA: The Food and Drug Administration Amendments Act of 2007, or FDAAA, significantly added to the FDA's authority to require post-approval studies. Under the FDAAA, if the FDA becomes aware of new safety information after approval of a product, they may require us to conduct further clinical trials to assess a known serious risk, signals of serious risk or to identify an unexpected serious risk. If required to conduct a post-approval study, periodic status reports must be submitted to the FDA. Failure to conduct such post-approval studies in a timely manner may result in administrative action being taken by FDA, including substantial civil fines.

Risk Evaluation and Mitigation Strategy Authority under FDAAA: The FDAAA also gave the FDA new authority to require the implementation of a Risk Evaluation and Mitigation Strategy, or REMS, for a product when necessary to minimize known and preventable safety risks associated with the product. The FDA may require the submission of a REMS before a product is approved, or after approval based on "new safety information," including new analyses of existing safety information. A REMS may include a medication guide, patient package insert, a plan for communication with healthcare providers, or other elements as the FDA deems are necessary to assure safe use of the product, which could include imposing certain restrictions on distribution or use of a product. A REMS must include a timetable for submission of assessments of the strategy at specified time intervals. Failure to comply with a REMS, including the submission of a required assessment, may result in substantial civil or criminal penalties.

Other Issues Related to Product Safety: Adverse events that are reported after marketing approval also can result in additional limitations being placed on a product's use and, potentially, withdrawal of the product from the market. In addition, under the FDAAA, the FDA has authority to mandate labeling changes to products at any point in a product's lifecycle based on new safety information derived from clinical trials, post-approval studies, peer-reviewed medical literature, or post-market risk identification and analysis systems data.

FDA Enforcement

The development of drug and biologic products, as well as the marketing of approved drugs and biologics, is subject to substantial continuing regulation by the FDA, including regulation of adverse event reporting, manufacturing practices and the advertising and promotion of the product. Failure to comply with the FDA and other governmental regulations can result in fines, unanticipated compliance expenditures, recall or seizure of products, total or partial suspension of production and/or distribution, suspension of the FDA's review of NDAs, BLAs, ANDAs or other product applications, enforcement actions, injunctions and criminal prosecution. Under certain circumstances, the FDA also has the authority to revoke previously granted drug approvals.

With respect specifically to information submitted to the FDA in support of marketing applications, the FDA, under its Fraud, Untrue Statements of Material Facts, Bribery and Illegal Gratuities Policy, can significantly delay the approval of a marketing application, or seek to withdraw an approved application where it identifies fraud or discrepancies in regulatory submissions. Such actions by the FDA may significantly delay or suspend substantive scientific review of a pending application during validity assessment or remove approved products from the market until the assessment is complete and questions regarding reliability of the data are resolved. In addition, the Generic Drug Enforcement Act of 1992 established penalties for wrongdoing in connection with the development or submission of an ANDA. Under this Act, the FDA has the authority to permanently or temporarily bar companies or individuals from submitting or assisting in the submission of an ANDA, and to temporarily deny approval and suspend applications to market generic drugs. The FDA may also suspend the distribution of all drugs approved or developed in connection with certain wrongful conduct and/or withdraw approval of an ANDA and seek civil penalties.

Healthcare Reform

Continuing studies of the proper utilization, safety and efficacy of pharmaceuticals and other health care products are being conducted by industry, government agencies and others. Such studies, which increasingly employ sophisticated methods and techniques, can call into question the utilization, safety and efficacy of previously marketed products and in some cases have resulted, and may in the future result, in the discontinuance of their marketing.

The Patient Centered Outcomes Research Institute (the "Institute"), a private, non-profit corporation created as a result of the PPACA, is tasked with assisting patients, clinicians, purchasers, and policy-makers in making informed health decisions. One of the Institute's initiatives will be to conduct comparative clinical effectiveness research, which is defined as "research evaluating and comparing health outcomes and the clinical effectiveness, risks, and benefits of two or more medical treatments, services, and items." It is important to note that the Institute would not be permitted to mandate coverage, reimbursement, or other policies for any public or private payer, however the outcome of the Institute's initiatives could influence prescriber behavior.

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Foreign Regulation

Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country/region to country/region, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement also may vary, sometimes significantly, from country/region to country/region.

Under the EU regulatory systems, we may submit marketing authorization applications either under a centralized procedure or decentralized procedure or the mutual recognition procedure. The centralized procedure is mandatory for medicines produced by a biotechnological process. The procedure is also mandatory for new active substances which are indicated for treatment of several diseases or conditions, including cancer and orphan conditions. Companies may apply for centralized assessment if the product contains a new active substance or the product constitutes significant therapeutic, scientific or technical innovation or the granting of authorization under the centralized procedure is in the interests of the EU patients. A centralized marketing authorization is valid in all EU member states. This marketing authorization is issued in the form of a European Commission decision which is legally binding in its entirety to which it is addressed.

Directive 2004/27/EC introduced two parallel procedures to the centralized procedure to allow a product to be progressively authorized in each of the member states of the EU. They are the decentralized procedure and the mutual recognition procedure. The mutual recognition procedure applies where the product has already been authorized in a member state of the EU that will act as reference member state. The national marketing authorization granted by the reference member state forms the basis for mutual recognition in the member states chosen by the applicant. In the decentralized procedure, the product in question is not authorized in any one the EU member states. In such a situation, the applicant company will request a member state to act as the reference member state to lead the scientific assessment for the benefit/risk balance for agreement by the concerned member states. In both cases, the concerned member states have up to 90 days to accept or raise reasoned objections to the assessment made by the reference member state.

In addition, pricing and reimbursement is subject to negotiation and regulation in most countries outside the U.S. Increasingly, adoption of a new product for use in national health services is subject to health technology assessment under the national rules and regulations to establish the clinical effectiveness and cost-effectiveness of a new treatment. In some countries, in order to contain health care expenditures, reference price is introduced in order for the national healthcare providers to achieve a price comparable to the reference price in the same therapeutic category. We may therefore face the risk that the resulting prices would be insufficient to generate an acceptable return to us.

Third Party Reimbursement and Pricing Controls

In the U.S. and elsewhere, sales of pharmaceutical products depend in significant part on the availability of reimbursement to the consumer from third-party payers, such as government and private insurance plans. Third-party payers are increasingly challenging the prices charged for medical products and services. It is time-consuming and expensive for us to go through the process of seeking reimbursement from Medicare and private payers. Our products may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

The PPACA enacted significant reforms, including revising the definition of “average manufacturer price” for reporting purposes, increasing Medicaid rebates, expanding the 340B drug discount program, and making changes to affect the Medicare Part D coverage gap, or “donut hole.” In the coming years, additional significant changes could be made to governmental healthcare programs, and the U.S. healthcare system as a whole, that may result in significantly increased rebates, decreased pricing flexibility, diminished negotiating flexibility, coverage and reimbursement limitations based upon comparative and cost-effectiveness reviews, and other measures that could significantly impact the success of our products.

In many foreign markets, including the countries in the EU, pricing of pharmaceutical products is subject to governmental control. In the U.S., there have been, and we expect that there will continue to be, a number of federal

and state proposals to implement similar governmental pricing control.

Employees

As of December 31, 2015, we had 212 employees (as compared to 241 employees as of December 31, 2014), 10 of whom hold an M.D. degree, and 18 of whom hold a Ph.D. degree. We believe that the success of our business will depend, in part, on

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our ability to attract and retain uniquely qualified personnel. Our employees are not part of any collective bargaining agreements, and we believe that we have good relations with our employees.

General Information

We are a Delaware corporation. We originally incorporated in Colorado in December 1987 as Americus Funding Corporation. We changed our corporate name in August 1996 to NeoTherapeutics, Inc., and reincorporated in Delaware in June 1997. We changed our corporate name in December 2002 to Spectrum Pharmaceuticals, Inc.

Our principal executive office is located at 11500 South Eastern Avenue, Suite 240, Henderson, Nevada 89052. Our telephone number is (702) 835-6300. Our website is located at www.sppirx.com. The information that can be accessed through our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part hereof.

We make our proxy statements, annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K (and related amendments to these reports, as applicable) available on our website free of charge as soon as practicable after filing or furnishing with the SEC.

All such reports are also available free of charge via EDGAR through the SEC website at www.sec.gov. In addition, the public may read and copy materials filed by us with the SEC at the SEC's public reference room located at 100 F Street, NE, Washington, D.C., 20549. Information regarding operation of the SEC's public reference room can be obtained by calling the SEC at 1-800-732-0330.

ITEM 1A. RISK FACTORS

Before deciding to invest in our company, or to maintain or increase your investment, you should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10-K and other reports we have filed with the SEC. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us, or that we currently deem immaterial, may also affect our business operations. If any of these risks are realized, our business, financial condition, or results of operations could be seriously harmed and in that event, the market price for our common stock could decline, and you may lose all or part of your investment.

These risk factors should be considered in connection with evaluating the forward-looking statements contained in this Annual Report on Form 10-K. These factors could cause actual results and conditions to differ materially from those projected in our forward-looking statements.

Risks Related to Our Business

Wholesaler actions could increase competitive and pricing pressures on pharmaceutical manufacturers, including us.

We sell certain of our products primarily through wholesalers, who in turn sell to end-users. These wholesalers comprise a significant part of the distribution network for pharmaceutical products in the U.S. A small number of large wholesalers control a significant share of the market, which can increase competitive and pricing pressures on pharmaceutical manufacturers, including us. In addition, wholesalers may apply pricing pressure through their fee-for-service arrangements.

We are aware of several competitors attempting to develop and market products competitive to our products, which may reduce or eliminate our commercial opportunities.

The pharmaceutical and biotechnology industries are intensely competitive and subject to rapid and significant technological changes, and a number of companies are pursuing the development of pharmaceuticals and products that target the same diseases and conditions that our products target, including products currently commercialized. We cannot predict with accuracy the timing or impact of the introduction of potentially competitive products or their possible effect on our sales. Certain potentially competitive products to our products are in various stages of development, some of which have pending applications for approval with the FDA or have been approved by regulatory authorities in other countries. Also, there are many ongoing studies with currently marketed products and other developmental products, which may yield new data that could adversely impact the use of our products in their

current and potential future indications. The introduction of competitive products could significantly reduce our sales, which, in turn would adversely impact our financial and operating results.

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We are a small company relative to our principal competitors, and our limited financial resources may limit our ability to develop and market our drug products.

Many companies, both public and private, including well-known pharmaceutical companies and smaller niche-focused companies, are developing products to treat many, if not all, of the diseases we are pursuing or are currently distributing drug products that directly compete with the drugs that we sell or that we intend to develop, market and distribute. Many of these companies have substantially greater financial, research and development, manufacturing, marketing and sales experience and resources than us. As a result, our competitors may be more successful than us in developing their products, obtaining regulatory approvals and marketing their products to consumers.

Competition for branded or proprietary drugs is less driven by price and is more focused on innovation in the treatment of disease, advanced drug delivery and specific clinical benefits over competitive drug therapies. We may not be successful in any or all of our current clinical studies; or if successful, and if one or more of our drug products is approved by the FDA, we may encounter direct competition from other companies who may be developing products for similar or the same indications as our drug products.

Companies that have products on the market or in research and development that target the same indications as our products target include, among others, Astra Zeneca PLC, Bayer AG, Endo International plc, Eli Lilly and Co., Novartis AG, Genentech, Inc. (Roche), Bristol-Myers Squibb Company, GlaxoSmithKline, Biogen-IDEC Pharmaceuticals, Inc., OSI Pharmaceuticals, Inc. (Astellas Pharma), Cephalon, Inc. (Teva Pharmaceuticals), Sanofi-Aventis, Inc., Pfizer, Inc., Genta Incorporated, Merck, Celgene Corporation, BiPar Sciences, Inc., Genzyme Corporation, Shire Pharmaceuticals, AbbVie, Poniard Pharmaceuticals, Inc., and Johnson & Johnson, who may be more advanced in the development of competing drug products or are more established.

Many of our competitors are large and well-capitalized companies focusing on a wide range of diseases and drug indications, and have substantially greater financial, research and development, marketing, human and other resources than we do. Furthermore, large pharmaceutical companies have significantly more experience than we do in pre-clinical testing, human clinical trials and regulatory approval procedures, among other things.

Our dependence on key executives, scientists and sales and marketing personnel could impact the development and management of our business.

We are highly dependent upon our ability to attract and retain qualified scientific, technical sales and marketing and managerial personnel. There is intense competition for qualified personnel in the pharmaceutical and biotechnology industries, and we cannot be sure that we will be able to continue to attract and retain the qualified personnel necessary, particularly as business prospects change, for the development and management of our business. Although we do not believe the loss of one individual would materially harm our business, our business might be harmed by the loss of the services of multiple existing personnel, as well as the failure to recruit additional key scientific, technical and managerial personnel in a timely manner. Much of the know-how we have developed resides in our scientific and technical personnel and is not readily transferable to other personnel. While we have an employment agreement with our Chief Executive Officer, we do not have employment agreements with any of our other key scientific, technical, or managerial employees.

If the distributors that we rely upon to sell our products fail to perform, our business may be adversely affected.

Our success depends on the continued customer support efforts of our network of distributors. In the U.S., we sell our products to a small num