SPECTRUM PHARMACEUTICALS INC
Form 10-K
March 12, 2014

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

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

For the fiscal year ended December 31, 2013

¨ **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	93-0979187
(State or other jurisdiction of incorporation or organization)	(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 (§ 229.405 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 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, 2013, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant was $449,722,900 (based upon the $7.46 closing sale price for shares of the Registrant s Common Stock as reported by the NASDAQ Global Select Market on June 28, 2013, the last trading date of the Registrant s most recently completed second fiscal quarter).

As of February 28, 2014, approximately 65,287,782 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 2014 Annual Meeting of Shareholders, to be filed on or before April 30, 2014, 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). These forward looking statements are intended to qualify for the safe harbor from liability established by the Private Securities Litigation Reform Act of 1995 and speak only as of the time this Annual Report on Form 10-K was filed with the Securities and Exchange Commission, or SEC. You can identify forward-looking statements by the use of forward-looking terminology such as, believes, expects, may, will, intends, plans, should, c pro forma, anticipates, estimates, continues, or other variations thereof, including their use in the negative, or by discussions of strategies, opportunities, plans or intentions. In addition, any statements that refer to projections of our future financial performance, trends in our businesses, or other characterizations of future events or circumstances are forward-looking statements. We have based these forward-looking statements largely on our current expectations based on information currently available to us and projections about future events and trends affecting the financial condition of our business. These Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. Spectrum Pharmaceuticals, Inc. s actual results may differ materially from the results projected in the forward-looking statements. Factors that might cause such a difference include, but are not limited to:

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;

the difficulty in predicting the timing or outcome of product development efforts and regulatory approvals; and

demand and market acceptance for our approved products.

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 Spec 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

Spectrum Pharmaceuticals, Inc. and its wholly-owned subsidiaries (Spectrum , the Company , we , our , or us), is a biotechnology company wi fully integrated commercial and drug development operations with a primary focus in hematology and oncology. Our strategy is comprised of acquiring, developing and commercializing a broad and diverse pipeline of late-stage clinical and commercial products.

We currently market four oncology drugs:

FUSILEV injection for patients in the U.S. with advanced metastatic colorectal cancer and to counteract certain side effects of methotrexate therapy;

ZEVALIN injection for patients in the U.S. and various international markets with follicular non-Hodgkin s lymphoma;

FOLOTYN injection for patients in the U.S. with relapsed or refractory peripheral T-cell lymphoma; and

MARQIBO injection for patients in the U.S. with relapsed Philadelphia chromosome negative acute lymphoblastic leukemia.

We also have ongoing indication expansion studies with several of our marketed products, and a diversified pipeline of product candidates in advanced-stage Phase 2 and Phase 3 studies. We have assembled an integrated in-house scientific team, including formulation development, clinical development, medical affairs, regulatory affairs, biostatistics and data management, and have established a commercial infrastructure for the marketing of our drug products. We also leverage the expertise of our worldwide partners to assist in the execution of our business strategy described in detail below.

Business Strategy

Our business strategy is comprised of the following three initiatives:

Maximizing the revenue potential of our four currently-marketed drugs for the treatment of cancer.

Our near-term outlook largely depends on sales and marketing successes for our four marketed drugs. It is this base business, along with potential additional indications for these drugs, that provides the working capital needed to operate our daily business and provides the necessary capital for opportunistic acquisitions.

Developing and commercializing the drugs for the treatment of cancer within our pipeline.
Our strategy for our development portfolio is to focus on late-stage development drugs. We strive to complete clinical studies to demonstrate the safety and efficacy of these drugs in order to obtain regulatory approval in a timely manner. Upon obtaining approval, our sales and marketing function educates physicians on the safety of the drug and its effectiveness in treating patients for the approved indication, with the goal of achieving maximum commercial success.

Expanding our pipeline of development-stage and commercial-stage drugs through business development activities.
It is our goal to identify new strategic opportunities that are synergistic with our currently-marketed drugs. We will continue to (i) explore strategic collaborations as they relate to drugs that are either in clinical trials or are currently on the market, and (ii) identify and secure drugs that have significant growth potential through enhanced marketing and sales efforts and/or through pursuit of additional clinical development. We may also identify and pursue partnerships for out-licensing certain of our drugs in development.

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 2014*, 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 are expected to be diagnosed in 2014 and over 585,000 persons are expected to die from the disease in 2014. Anyone can develop cancer. Since the 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.

All cancers involve the malfunction of genes that control cell growth and division. Only a small proportion of cancers are strongly hereditary, in that an inherited genetic alteration confers a very high risk for developing cancer. Inherited factors play a larger role in determining risk for some cancers (e.g., colorectal, breast, and prostate) than for others. It is now thought that many familial cancers arise from the interplay between common gene variations and lifestyle/environmental risk factors. However, most cancers do not result from inherited genes but rather from damage to genes occurring during a person s lifetime. Genetic damage may result from internal factors, such as hormones or the metabolism of nutrients within cells, or external factors, such as tobacco, or excessive exposure to chemicals, sunlight, or ionizing radiation.

Cancer cell growth is different from normal cell growth. Instead of being regulated and stopping to grow in a controlled manner, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells do not do. Cells become cancer cells because of DNA damage. DNA is in every cell and it directs all of the cell s actions. In a normal cell, when DNA is damaged, the cell either repairs the damage, or the cell dies. In cancer cells, the damaged DNA is not repaired, and the cell doesn t die. Instead, it continues to make new cells in an uncontrolled manner that the body doesn t require. People can inherit abnormal DNA, but most DNA damage is caused by abnormal cellular reproduction, usually triggered by environmental causes. In most cases, the cancer cells form a tumor, though some cancers, like leukemia, involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body where they begin to grow and form new tumors. This happens when the cancer cells get into the body s bloodstream or lymph vessels; this process of cancer spreading is called metastasis. No matter where a cancer may spread, it is always named for the place where it originated. For example, breast cancer that has spread to the liver is called metastatic breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is called metastatic prostate cancer, not bone cancer. Different types of cancer can behave very differently. For instance, lung cancer and skin cancer are very different diseases. They grow at different rates and respond to different 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, and their approved indications, are summarized in the following table:

FUSILEV

FUSILEV (levoleucovorin), a novel folate analog formulation 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.
- for rescue after high-dose methotrexate therapy in osteosarcoma.
- to diminish the toxicity and counteract the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists.

The product similar to FUSILEV is marketed outside the U.S. by Pfizer, Sanofi-Aventis, and Takeda.

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 with relapsed or refractory peripheral T-cell lymphoma (PTCL). FOLOTYN was the first chemotherapy approved by the FDA 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 10 to 15% of all NHL cases in the United States.

Based on preclinical studies, we believe that FOLOTYN selectively enters cells expressing 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 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 will be testing 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. Rituximab is used to reduce the number of B-cells in the blood and Y-90 ZEVALIN is then given to treat non-Hodgkin s lymphoma. 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 the treatment of patients with:

Recurring, low-grade or follicular B-cell NHL, after other anticancer drugs are no longer working.

Newly diagnosed follicular NHL following a response to initial anticancer therapy.

We are currently working towards a new indication for ZEVALIN for diffuse large B-cell lymphoma (DLBCL). An estimated 40,000 new cases of DLBCL were diagnosed in major markets in 2010. The need for improved treatments for DLBCL is high because the two-year progression-free survival rate is only approximately 55% and the estimated two-year overall survival rate is 71%.

ZEVALIN would be used as an add-on to frontline therapy in which there is currently no competitor. A number of Phase 2 studies have been completed by investigators with high response rates in this indication. We plan to complete our Phase 3 study enrollment in early 2016 and file a supplemental Biologics License Application (sBLA) in 2018.

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 Philadelphia chromosome-negative acute lymphoblastic leukemia (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. During 2014, we also intend to conduct an additional Phase 2 study for MARQIBO in patients with NHL.

Product Pipeline

BELEODAQ

BELEODAQ (belinostat) is a histone deacytelase, (HDAC) inhibitor that is being studied in multiple clinical trials, both as a single drug and in combination with chemotherapeutic drugs for the treatment of various hematological and solid tumors. Its 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. We are currently seeking FDA approval for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma.

BELEODAQ is differentiated from other HDAC inhibitors that selectively inhibit a single class of HDAC enzymes because it inhibits all 3 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.

Based on the data from the clinical studies, we believe there are many potential attributes associated with BELEODAQ 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-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. Hence, BELEODAQ is currently being investigated in multiple indications, both as monotherapy and in combination with other treatment regimens. Numerous studies have been conducted, or are ongoing, through the National Cancer Institute (the NCI) and other well-known oncologic academic institutions. Additionally, we have a comprehensive development plan for BELEODAQ, which includes both hematologic indications, such as PTCL, and solid tumor indications, such as ovarian cancer, colorectal cancer and non-small cell lung cancer. Based upon the foregoing, we believe BELEODAQ potentially has broad applicability and hence, commercial potential beyond that of its currently targeted indication.

BELEODAQ is currently the only HDAC inhibitor in clinical development with multiple potential routes of administration, including intravenous administration, continuous intravenous infusion and oral administration, which we believe may afford BELEODAQ a significant competitive advantage.

In December 2013, we filed our NDA with the FDA. Our application was subsequently accepted by the FDA with Priority Review in February 2014.

Captisol-Enabled® MELPHALAN

Captisol-enabled MELPHALAN (C-E MELPHALAN) is a novel intravenous formulation of MELPHALAN that has the potential to offer multiple advantages for clinicians and patients in the multiple myeloma transplant setting. Multiple myeloma is a cancer of plasma cells, a type of white blood cell present mainly in the bone marrow that produces antibodies. In multiple myeloma, 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. Per NCI and the ACS, there were an estimated 22,000 new cases of multiple myeloma in the U.S. in 2013, with the incidence of new cases increasing by approximately 1.7% per year. The current intravenous MELPHALAN market is approximately $130 million annually, with predominant use in stem cell transplants. The rate of autologous stem cell transplantation for patients with multiple myeloma is growing by approximately 3.3% annually.

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

C-E MELPHALAN was granted Orphan Drug status by the FDA for use as a high-dose conditioning regimen prior to hematopoietic progenitor (stem) cell transplantation. If approved, the propylene glycol-free formulation of MELPHALAN will be the first product approved for this indication.

Currently, C-E MELPHALAN is a Phase 2B drug (Pivotal Trial) with an NDA filing anticipated in 2014.

APAZIQUONE

APAZIQUONE is an anti-cancer agent that becomes activated by certain enzymes often present in higher amounts in cancer cells than in normal cells. It is currently being investigated for the treatment of Non- muscle Invasive Bladder Cancer (NMIBC), which is a cancer that is only in the innermost layer of the bladder and has not spread to deeper layers of the bladder.

The ACS estimated that the 2013 incidence and prevalence of bladder cancer in the U.S. was approximately 74,690 and over 500,000 respectively. According to Botteman et al., (PharmacoEconomics 2003), bladder cancer is the most expensive cancer to treat on a lifetime basis.

The initial treatment of this cancer is to attempt a complete surgical removal of the tumor. However, bladder cancer is a highly recurrent disease with approximately 75% of patients recurring within 5 years, and a majority of patients recurring within 2 years. This high recurrence rate is attributed to:

(1) the highly implantable nature of cancer cells that are dispersed during surgery,

(2) incomplete tumor resection, and

(3) 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.

APAZIQUONE is a bio-reductive alkylating indoloquinone that is enzymatically activated by enzymes that are over expressed by bladder tumors that is being tested in NMIBC. Pharmacokinetic studies have verified that APAZIQUONE 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. APAZIQUONE 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 APAZIQUONE are distinct from other intravesical agents currently in use for the treatment of recurrent bladder cancer. An immediate instillation of APAZIQUONE may help by:

(1) reducing tumor recurrence by destroying dispersed cancer cells that would otherwise re-implant onto the inner lining of the bladder,

(2) by destroying remaining cancer cells at the site of tumor resection (also known as chemo-resection), and

(3) by destroying tumors not observed during resection (also known as chemo-ablation).

We expect to commence a confirmatory Phase 3 study for APAZIQUONE in 2014 and expect to prepare and submit a NDA at the end of 2014.

SPI-2012

SPI-2012, our third biologic drug, is used for the treatment of chemotherapy-induced neutropenia. In January 2012, we entered into a co-development and commercialization agreement with Hanmi Pharmaceutical Company, 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 market for GCSF-related drugs was over $5.0 billion in 2013.

We are currently enrolling a Phase 2 study with clinical trial results expected in the second half of 2014.

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 for our products. However, we have only one approved contract manufacturer for each aspect of the manufacturing process for ZEVALIN and MARQIBO. We have multiple drug product contract manufacturers for FUSILEV and FOLOTYN.

We believe these third-party manufacturers have the capability to meet our projected worldwide clinical trial and commercial requirements for our products. We attempt to prevent disruption of supplies through supply agreements, appropriate forecasting, maintaining stock levels and other strategies. We believe that the market for such manufacturers and suppliers is such 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 market and sell our drugs through a direct sales force in the U.S., and through distributors in Europe and Japan. We divide the U.S. market between corporate accounts and oncology accounts. The primary decision makers for our products are oncologists and hematologists. As of December 31, 2013, our U.S. sales force (management, representatives, and direct support) numbered 81 employees.

Our corporate accounts are divided among four regions and 20 territories, led by our Vice President of Corporate Accounts and Executive Director of Corporate Accounts Sales. Each region is managed by an Associate Director of Corporate Accounts who oversees four Regional Business Managers.

Our oncology accounts are divided among six regions and 40 territories, led by our Vice President of Sales. Each region is managed by a Regional Sales Director who oversees six or seven Oncology Account Managers (sales representatives), an Oncology Nurse Specialist (sales support), and a Clinical Logistical Specialist (sales support).

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 product sales in 2013, 2012, and 2011 are as follows:

	2013	2012	2011
Oncology Supply	35.4%	26.5%	57.0%
McKesson Specialty	19.8%	23.2%	19.1%
ICS	15.8%	19.4%	*
Cardinal Health	*	15.7%	*

* 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, 2013 and 2012 are as follows:

	December 31, 2013	December 31, 2012
Oncology Supply	37.7%	37.7%
McKesson Specialty	30.7%	26.0%
ICS	10.3%	19.1%

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 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 product targets include, among others, Astra Zeneca PLC, Bayer AG, Endo Pharmaceuticals, Inc., 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, Abbott Laboratories, 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.

The general competitive landscape for each of our commercialized products is summarized below:

(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 three generic companies approved by the FDA to sell the leucovorin product, we are competing with a low-cost alternative.

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

Rituxan® (rituximab), marketed by Genentech and Biogen, 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.

Bexxar® therapeutic regimen (Tositumomab and Iodine I ^{131} Tositumomab), a radiopharmaceutical marketed by GlaxoSmithKline, is indicated for the treatment of patients with CD20 antigen-expressing relapsed or refractory, low-grade, follicular, or transformed NHL, including patients with Rituximab-refractory NHL. In August 2013, the manufacturer of this product announced the discontinuation of both the manufacture and sale of Bexxar as of February 20, 2014.

(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.

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 BELEODAQ and alisertib, which, if approved, may compete with FOLOTYN in the United States. 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 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.

Research and Development

New drug development is the process whereby drug product candidates are tested for the purpose of filing a new drug application (NDA) or a Biologistics License Application (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 personnel expenses, contract services, license fees and milestone payments, clinical trials, laboratory supplies and drug products, and certain allocations of corporate costs. The below table summarizes our research and development expenses by project in 2013, 2012, and 2011:

	Research and Development Expenses for the Year Ended December 31, (in thousands)		
	2013	2012	2011
APAZIQUONE	$ 1,078	$ 6,642	$ 7,695
BELEODAQ	6,733	3,742	7,207
FUSILEV	4,517	1,416	1,239
FOLOTYN			