

SPECTRUM PHARMACEUTICALS INC

Form 10-K

March 14, 2017

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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

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

For the fiscal year ended December 31, 2016

☐ 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 (I.R.S. Employer
incorporation or organization) 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 ☒

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or 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 ☒ No ☐

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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 ☒ No ☐

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

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

Large accelerated filer ☐

Accelerated filer ☐

☒

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

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

As of June 30, 2016, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant was \$424,190,348 (based upon the \$6.57 per share closing sale price for shares of the Registrant's Common Stock as reported by the NASDAQ Global Select Market on June 30, 2016, the last trading date of the Registrant's most recently completed second fiscal quarter).

As of February 28, 2017, approximately 80,252,585 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 2017 Annual Meeting of Stockholders, to be filed on or before May 1, 2017 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, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934 as amended, or 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 and revenue assumptions, clinical studies, including designs and implementation, development timelines, product acquisitions, litigation and regulatory actions, 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 negative thereof or 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;

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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.

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.

Spectrum Pharmaceuticals, Inc.®, FUSILEV®, FOLOTYN®, ZEVALIN®, MARQIBO®, BELEODAQ®, and EVOMELA®. ROLONTIS™, QAPZOLA™, REDEFINING CANCER CARE™ and the Spectrum Pharmaceuticals' logos are trademarks owned by Spectrum Pharmaceuticals, Inc. Any other trademarks are the property of their respective owners.

PART I

ITEM 1. BUSINESS

Company Overview

Spectrum Pharmaceuticals, Inc. is a biotechnology company, with a primary strategy comprised of acquiring, developing, and commercializing a broad and diverse pipeline of late-stage clinical and commercial products. We have an in-house clinical development organization with regulatory and data management capabilities, a commercial infrastructure, and a field sales force for our marketed products. Currently, we have six approved oncology/hematology products that target different types of cancer including: non-Hodgkin's lymphoma, or NHL, advanced metastatic colorectal cancer, or mCRC, acute lymphoblastic leukemia, or ALL, and multiple myeloma, or MM.

We also have three drugs in mid-to-late stage development (defined as Phase 2 and Phase 3):

• ROLONTIS (previously referred to as SPI-2012 or LAPS-G-CSF) for chemotherapy-induced neutropenia.

• QAPZOLA (previously referred to as APAZQUONE) for immediate intravesical instillation in post-transurethral resection of bladder tumors in patients with non-muscle invasive bladder cancer, or NMIBC.

• POZIOTINIB, a novel pan-HER inhibitor used in the treatment of patients with a variety of solid tumors, including breast and lung 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 cancer 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.

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According to the American Cancer Society's publication Cancer Facts & Figures 2016, 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 2016 and over 596,000 persons were expected to die from the disease. 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.

Product Portfolio

We have a product portfolio consisting of both commercial stage and development stage products that address various cancer types (see the section titled Research and Development below for our pipeline of cancer therapeutics that are in various development stages). Our commercialized products and products in development may have serious adverse effects, or SAEs, that could result in a negative impact on sales and delays, or removal of regulatory approval. For further information on these SAEs, see the risk factor within accompanying Item 1A. Risk Factors – Risks Related to Our Business --Reports of adverse events or safety concerns involving each of our products or similar agents, sold by us or our development partners and/or licensees, could delay or prevent us from obtaining or maintaining regulatory approval or negatively impact sales.

We remain committed to growing the sales of our currently marketed products, as we strive to maintain a robust development pipeline to deliver important options for patients suffering from cancer, as discussed below.

Commercialized Products

FUSILEV

FUSILEV (levoleucovorin) is 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 mCRC;
- for rescue after high-dose methotrexate, or MTX, therapy in osteosarcoma; and
- to diminish the toxicity and counteract the effects of impaired MTX 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., or 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, or 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 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, or B-cells, and T-lymphocytes, or T-cells.

PTCL comprises a group of rare and aggressive NHLs that develop from mature T-cells and 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, or RFC-1, a protein that is frequently over expressed on cancer cells compared to normal cells. Once inside cancer cells,

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FOLOTYN is efficiently polyglutamylated and retained inside the cells for a longer time. FOLOTYN and its polyglutamates inhibit dihydrofolate reductase, or DHFR, an enzyme critical in the folate pathway, thereby interfering with DNA and RNA synthesis and triggering cancer cell death.

The safety and efficacy of FOLOTYN was evaluated in an open-label, single-arm, multi-center, international trial that enrolled patients with relapsed or refractory PTCL. One hundred and eleven patients were treated with FOLOTYN at 30 mg/m² once weekly by IV push over three to five minutes for six weeks in seven-week cycles until disease progression or unacceptable toxicity. Of the 111 patients treated, 109 patients were evaluable for efficacy. The primary efficacy endpoint was overall response rate (complete response, complete response unconfirmed, and partial response) as assessed by International Workshop Criteria, or IWC. Of the 109 evaluable patients, 27% of patients achieved a response that met these criteria.

In addition to its approved indication, FOLOTYN is being investigated in a Phase 1 study in combination with the CHOP chemotherapy regimen. Once the proper dose of FOLOTYN in combination with CHOP has been determined, we expect to plan a Phase 3 study of the combinations of FOLOTYN and CHOP, and BELEODAQ and CHOP, compared to CHOP alone for the treatment of first line PTCL. The Phase 1 study and the Phase 3 study concept are also the current post-marketing requirements for the FDA's accelerated approval of our currently marketed indication for FOLOTYN.

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, or NCI, estimated 73,000 new cases of NHL in the U.S. in 2016. 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 was studied in an international, open-label, multi-center, single-arm trial. Eligible patients were 18 years of age or older with Philadelphia chromosome negative ALL in second or greater relapse or whose disease progressed after two or greater treatment lines of anti-leukemia therapy. Patients received intravenous MARQIBO monotherapy at 2.25 mg/m² over 60 minutes every seven days. The treated population included 65 patients who received at least one dose of MARQIBO. Of the 65 evaluable patients, three (4.6%) achieved complete remission, or CR, seven (10.8%) achieved complete remission with incomplete blood count recovery, or CRi, for a total of 10 (15.4%) total patients receiving a CR or CRi.

In addition to its approved indication, MARQIBO is being investigated in pediatric ALL in a Phase 1 investigator-initiated study in the United States. Based on data from this study, Spectrum will determine whether to conduct a registration study for MARQIBO in this setting. We are in discussions with the FDA regarding the possibility of using this development plan to satisfy one of the post-marketing requirements for the accelerated approval of our currently marketed indication for MARQIBO.

MARQIBO is also being investigated in diffuse large B-cell lymphoma in a Phase 3 investigator-initiated study in Europe in combination with the standard CHOP chemotherapy regimen in Europe, CHOP-14. Based on interim data from this study, Spectrum will consider whether to conduct a study of the combination of MARQIBO with the standard CHOP regimen in the United States, CHOP-21.

BELEODAQ

BELEODAQ (belinostat) is a histone deacytelase, or 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

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angiogenesis, induction of differentiation, and the activity in tumors that had become resistant to anticancer agents such as the platinum, taxanes, and topoisomerase II inhibitors.

The safety and effectiveness of BELEODAQ was evaluated in an open-label, single-arm, non-randomized international trial involving 129 participants with relapsed or refractory PTCL. Patients were treated with BELEODAQ 1,000 mg/m² administered over 30 minutes via IV infusion once daily on days one to five of a 21-day cycle until disease progression or unacceptable toxicity. The primary efficacy endpoint was response rate (complete response and partial response) as assessed by an independent review committee, or IRC, using the International Workshop Criteria, or IWC. In all evaluable patients (N = 120) treated with BELEODAQ, the overall response rate per central review using IWC was 25.8%.

We market FOLOTYN and BELEODAQ for the treatment of relapsed or refractory PTCL. These drugs have different mechanisms of action, and as a result, the treating physician may prefer to start treatment with one drug over the other. In addition, physicians may prefer one drug over another based on specific patient factors such as the subtype of PTCL being treated, existing comorbidities, or the performance status of the patient. However, both drugs have similar response rates of approximately 25-30%. It is common for patients to cycle through multiple drugs, including both FOLOTYN and BELEODAQ, though these drugs are not FDA-approved for use in combination with one another.

In addition to its approved indication, BELEODAQ has been investigated in a Phase 1 study in combination with the CHOP chemotherapy regimen. Once the proper dose of FOLOTYN in combination with CHOP has been determined, we expect to plan a Phase 3 study of the combination of BELEODAQ and CHOP and FOLOTYN and CHOP, compared to CHOP alone for the treatment of first line PTCL. The Phase 1 study and the Phase 3 study concept are also the current post-marketing requirements for the FDA's accelerated approval of our currently marketed indication for BELEODAQ.

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

EVOMELA is intended for use as a high-dose conditioning treatment prior to autologous stem cell transplant, or ASCT, 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 30,000 new cases of MM in the U.S. in 2016, with the incidence of new cases increasing by approximately 2% per year.

The EVOMELA formulation avoids the use of propylene glycol, or PG, which is required as a co-solvent in the currently-available formulation of this product. The use of Betadex Sulfobutyl Ether Sodium technology to reformulate EVOMELA may allow for longer administration durations and slower infusion rates, potentially enabling clinicians to avoid reductions.

On March 10, 2016, the FDA approved 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. In April 2016, we launched EVOMELA, our sixth anti-cancer drug, with our existing sales force. On April 12, 2016, the FDA granted orphan drug exclusivity to EVOMELA, giving us seven years of marketing exclusivity until March 10, 2023. We also have two composition of matter patents that do not expire until March 2029.

EVOMELA was approved by the FDA based on its bioequivalence to the standard melphalan formulation (Alkeran) via the new drug regulatory pathway provided by Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act. The safety and effectiveness of EVOMELA in high-dose conditioning treatment was evaluated in an open-label, single-arm, non-randomized trial. The objective of the trial was to determine the overall safety and toxicity profile of 200 mg/m² of EVOMELA in patients with MM undergoing ASCT. The overall response rate (partial response or better) improved from 79% prior to the ASCT procedure to 95% at 90 to 100 days post-transplant. There was also an

increase in the number of patients with a stringent complete response from zero patients prior to the ASCT procedure to 16% at 90 to 100 days post-transplant. Myeloablation, neutrophil engraftment, and platelet engraftment were achieved by all 61 patients. Myeloablation occurred on day five of ASCT (range ASCT days -one to six) with the median time to myeloablation from dosing of eight days. The median time to neutrophil engraftment was 12 days (range ASCT days 10 to 16). The median time to platelet engraftment was 13 days (range ASCT days 10 to 28).

New Product Pipeline

ROLONTIS

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ROLONTIS 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., or Hanmi, for ROLONTIS 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 chemotherapy treatments.

Neutropenia, a common side effect of chemotherapy, is a condition where the number of neutrophils or white blood cells are too low, and can lead to infection, hospitalization, and even death. Granulocyte colony-stimulating factor, or G-CSF, stimulates the production of white blood cells by the bone marrow. A recombinant form of G-CSF 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 G-CSF-related drugs is over \$6 billion.

A Phase 2 clinical study of ROLONTIS was completed. This study assessed the effect of three different doses of this compound relative to pegfilgrastim (Neulasta, an approved long lasting G-CSF). The primary endpoint of the study was the duration of severe neutropenia (defined as absolute neutrophil count is $<0.5 \times 10^9/L$) during Cycle 1 in patients with early stage breast cancer who are treated with docetaxel and cyclophosphamide (TC). The Phase 2 study demonstrated ROLONTIS to be non-inferior to 6 mg of pegfilgrastim at the 135 mcg/kg dose (0.44 days versus 0.31 days) and superior to pegfilgrastim at the 270 mcg/kg dose (0.03 days versus 0.31 days). The adverse event incidences were comparable to pegfilgrastim in all doses tested.

In September 2014, we announced our decision to advance ROLONTIS to Phase 3 trials due to the positive Phase 2 results in our collaboration program with Hanmi, and began discussions with the FDA and the European Medicines Agency, or EMA, to discuss our Phase 3 trial design. In December 2015, we reached agreement with the FDA regarding our Phase 3 Special Protocol Assessment, or SPA, for ROLONTIS. This pivotal Phase 3 study (ADVANCE Study, or SPI-GCF-301) was initiated in the first quarter of 2016 to evaluate ROLONTIS as a treatment for chemotherapy-induced neutropenia in patients with breast cancer. The study uses a fixed dose of ROLONTIS and is randomized to be compared to Neulasta with non-inferiority of duration of severe neutropenia as the primary endpoint. This study will be conducted in the United States, Canada, and South Korea. A second pivotal Phase 3 study (RECOVER Study, or SPI-GCF-302) with an identical study design is also planned. This study will enroll patients globally including in Europe and the United States.

QAPZOLA

QAPZOLA 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.

The NCI estimates that the 2016 incidence and prevalence of bladder cancer in the U.S. was approximately 77,000 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. QAPZOLA represents much needed therapy for patients and may provide a meaningful opportunity to reduce overall medical costs.

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Pharmacokinetic studies have verified that QAPZOLA 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. QAPZOLA 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. An immediate instillation of QAPZOLA 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).

We submitted a New Drug Application, or NDA, on December 11, 2015 which was accepted on February 9, 2016. On November 17, 2016, we received a Complete Response Letter, or CRL. We have since developed a new Phase 3 study for QAPZOLA, and in February 2017, we received a SPA from the FDA. The new Phase 3 study has been specifically designed to build on learnings from the previous studies as well as recommendations from the FDA. Compared to the previous study, this study will use twice the dosage of QAPZOLA (8mg), will evaluate approximately 70% fewer patients (n=425), and will also evaluate time-to-recurrence as the primary endpoint compared to recurrence at two years.

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, 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. In two Phase 1 studies for this drug that enrolled a variety of solid tumor patients and tested a variety of doses and schedules for POZIOTINIB, 6 of 10 breast cancer patients who failed at least two prior lines of anti-HER2 therapy demonstrated a partial response. The safety profile was consistent with similar drugs in this class with four patients having a grade 3 diarrhea response.

In November 2015, we submitted an Investigational New Drug, or IND, application with the FDA. In March 2016, we initiated a Phase 2 Breast Cancer Trial. The Phase 2 study (SPI-POZ-201) is an open-label study that will enroll approximately 75 patients with HER-2 positive metastatic breast cancer, who have failed at least two and no more than four HER-2 directed therapies. The dose and schedule of oral POZIOTINIB is based on clinical experience from the studies in South Korea, and in addition, include the use of prophylactic therapies to help minimize known side-effects of pan-HER directed therapies.

In collaboration with The University of Texas MD Anderson Cancer Center, an investigator sponsored trial is being initiated in non-small cell lung cancer patients with EGFR Exon 20 insertion mutations. The study is expected to yield results before December 31, 2017.

For information on operating revenue related to the Company's principal products, as well as net loss, see Item 8 of Part II to this Annual Report on Form 10-K. Additionally, for information regarding possible adverse events or safety concerns regarding our commercialized and development stage products, see Item 1A. Risk Factors - Reports of adverse events or safety concerns involving each of our products or similar agents, sold by us or our development partners and/or licensees, could delay or prevent us from obtaining or maintaining regulatory approval or negatively impact sales.

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, or 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.

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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” that generally serve different end-user types. The primary decision makers for our products are oncologists and hematologists. As of December 31, 2016, our U.S. sales force (sales management, sales representatives, and sales administrative support) numbered 92 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 2016, 2015, and 2014 are as follows:

	Product Sales		
	2016	2015	2014
AmerisourceBergen Corporation, and its affiliates	38.4%	36.7%	40.4%
McKesson Corporation and its affiliates	31.0%	34.2%	32.9