ALEXION PHARMACEUTICALS INC
Form 10-K
February 16, 2017

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, 2016
or
¨Transition report pursuant to Section 13 or 15 (d) of the Securities Exchange Act of 1934
For the transition period from to
Commission file number: 0-27756

ALEXION PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	13-3648318
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

100 College Street, New Haven, Connecticut 06510
(Address of Principal Executive Offices) (Zip Code)
475-230-2596
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act: Common Stock, par value $0.0001

Name of each exchange on which registered: The NASDAQ Stock Market LLC
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 Website, 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 (§ 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 x 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 Act). Yes ¨ No x

The aggregate market value of the Common Stock held by non-affiliates of the registrant, based upon the last sale price of the Common Stock reported on The NASDAQ Stock Market LLC on June 30, 2016, was $25,314,108,813.(1)

The number of shares of Common Stock outstanding as of February 13, 2017 was 224,613,750.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement to be used in connection with its Annual Meeting of Stockholders to be held on May 10, 2017, are incorporated by reference into Part III of this report.

(1) Excludes 7,417,897 shares of common stock held by directors and executive officers at June 30, 2016. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, directly or indirectly, to direct or cause the direction of the management or policies of the registrant, or that such person is controlled by or under common control with the registrant.

Alexion Pharmaceuticals, Inc.
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PART I

Unless the context requires otherwise, references in this report to “Alexion”, the “Company”, “we”, “our” or “us” refer to Alexion Pharmaceuticals, Inc. and its subsidiaries.

Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that have been made pursuant to the provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements are based on current expectations, estimates and projections about our industry, management’s beliefs, and certain assumptions made by our management, and may include, but are not limited to, statements regarding the potential benefits and commercial potential of Soliris®, Strensiq® and Kanuma® for approved indications and any expanded uses, timing and effect of sales of our products in various markets worldwide, pricing for our products, level of insurance coverage and reimbursement for our products, level of future product sales and collections, timing regarding development and regulatory approvals for additional indications or in additional territories, the medical and commercial potential of additional indications for Soliris, failure to satisfactorily address the issues raised by the U.S. Food and Drug Administration (FDA) in the March 2013 Warning Letter and Form 483s issued by the FDA, costs, expenses and capital requirements, cash outflows, cash from operations, status of reimbursement, price approval and funding processes in various countries worldwide, progress in developing interest about our products and our product candidates in the patient, physician and payer communities, the safety and efficacy of our products and our product candidates, estimates of the potential markets and estimated commercialization dates for our products and our product candidates around the world, sales and marketing plans, any changes in the current or anticipated market demand or medical need for our products or our product candidates, status of our ongoing clinical trials for eculizumab, asfotase alfa, sebelipase alfa and our other product candidates, commencement dates for new clinical trials, clinical trial results, evaluation of our clinical trial results by regulatory agencies, the adequacy of our pharmacovigilance and drug safety reporting processes, prospects for regulatory approval of our products and our product candidates, need for additional research and testing, the uncertainties involved in the drug development process and manufacturing, performance and reliance on third party service providers, our future research and development activities, plans for acquired programs, our ability to develop and commercialize products with our collaborators, assessment of competitors and potential competitors, the outcome of challenges and opposition proceedings to our intellectual property, assertion or potential assertion by third parties that the manufacture, use or sale of our products infringes their intellectual property, estimates of the capacity of manufacturing and other service facilities to support our products and our product candidates, potential costs resulting from product liability or other third party claims, the sufficiency of our existing capital resources and projected cash needs, the possibility that expected tax benefits will not be realized, assessment of impact of recent accounting pronouncements, declines in sovereign credit ratings or sovereign defaults in countries where we sell our products, delay of collection or reduction in reimbursement due to adverse economic conditions or changes in government and private insurer regulations and approaches to reimbursement, uncertainties surrounding legal proceedings, company investigations and government investigations, including our Securities and Exchange Commission (SEC) and U.S. Department of Justice (DOJ) investigations, the securities fraud class action litigation filed in December 2016, the investigation by our Audit and Finance Committee announced November 2016 (the Audit Committee Investigation), and the inquiry by the U.S. Attorney’s Office for the District of Massachusetts requesting documents relating generally to our support of patient assistance programs, risks related to potential disruptions to our business as a result of the leadership changes and transition announced in December 2016, the risk that hiring a new CEO may take longer than anticipated, the short and long-term effects of other government healthcare measures, and the effect of shifting foreign exchange rates. Words such as “anticipates,” “expects,” “intends,” “plans,” “believes,” “seeks,” “estimates,” variations of such words and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements are not guarantees of future performance and are subject to certain risks, uncertainties, and assumptions that are difficult to predict; therefore, actual results may differ materially from those expressed or forecasted in any such forward-looking statements. Such risks and uncertainties include, but are not limited to, those discussed later in this report under the section entitled “Risk Factors”. Unless required by law, we undertake no obligation to update publicly any forward-looking statements, whether because of new information, future events or otherwise. However, readers should

carefully review the risk factors set forth in this and other reports or documents we file from time to time with the SEC.

Item 1. BUSINESS.
(dollars and shares in millions)

Overview
We are a biopharmaceutical company focused on serving patients with devastating and ultra-rare disorders through the innovation, development and commercialization of life-transforming therapeutic products.

In our complement franchise, Soliris® is the first and only therapeutic approved for patients with either paroxysmal nocturnal hemoglobinuria (PNH), a life-threatening and ultra-rare genetic blood disorder, or atypical hemolytic uremic syndrome (aHUS), a life-threatening and ultra-rare genetic disease. PNH and aHUS result from chronic uncontrolled activation of the complement component of the immune system.

In our metabolic franchise, we commercialize Strensiq® for the treatment of patients with Hypophosphatasia (HPP) and Kanuma® for the treatment of patients with Lysosomal Acid Lipase Deficiency (LAL-D). HPP is an ultra-rare genetic disease characterized by defective bone mineralization that can lead to deformity of bones and other skeletal abnormalities. LAL-D is a serious, life threatening ultra-rare disease in which genetic mutations result in decreased activity of the Lysosomal Acid Lipase (LAL) enzyme leading to marked accumulation of lipids in vital organs, blood vessels and other tissues.

We are also evaluating additional potential indications for eculizumab in other severe and devastating diseases in which uncontrolled complement activation is the underlying mechanism, and we are progressing in various stages of development with additional product candidates as potential treatments for patients with devastating and ultra-rare disorders.

We were incorporated in 1992. In June 2015, we acquired all of the outstanding shares of common stock of Synageva BioPharma Corp. (Synageva), a publicly-held clinical-stage biotechnology company. The acquisition furthered our objective to develop and commercialize life-transforming therapies for patients with devastating and ultra-rare diseases.

Products and Development Programs

We focus our product development programs on life-transforming therapeutics for devastating and ultra-rare diseases for which current treatments are either non-existent or inadequate.

Marketed Products

Our marketed products include the following:

Product	Development Area	Indication
Soliris (eculizumab)	Hematology	Paroxysmal Nocturnal Hemoglobinuria (PNH)
	Hematology/Nephrology	Atypical Hemolytic Uremic Syndrome (aHUS)
Strensiq (asfotase alfa)	Metabolic Disorders	Hypophosphatasia (HPP)
Kanuma (sebelipase alfa)	Metabolic Disorders	Lysosomal Acid Lipase Deficiency (LAL-D)

Soliris (eculizumab)

Soliris is designed to inhibit a specific aspect of the complement component of the immune system and thereby treat inflammation associated with chronic disorders in several therapeutic areas, including hematology, nephrology, neurology and transplant rejection. Soliris is a humanized monoclonal antibody that effectively blocks terminal complement activity at the doses currently prescribed. The initial indication for which we received approval for Soliris is PNH.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

PNH is a debilitating and life-threatening, ultra-rare genetic blood disorder defined by chronic uncontrolled complement activation leading to the destruction of red blood cells (hemolysis). The chronic hemolysis in patients with PNH may be associated with life-threatening thromboses, recurrent pain, kidney disease, disabling fatigue, impaired quality of life, severe anemia, pulmonary hypertension, shortness of breath and intermittent episodes of dark-colored urine (hemoglobinuria). We continue to work with researchers to expand the base of knowledge in PNH and the utility of Soliris to treat patients with PNH. Soliris is approved for the treatment of PNH in the United States (U.S.), Europe, Japan and in several other territories. We are sponsoring a multinational registry to gather information regarding the natural history of patients with PNH and the longer term outcomes during Soliris treatment. In addition, Soliris has been granted orphan drug designation for the treatment of PNH in the U.S., Europe, Japan and several other territories.

Atypical Hemolytic Uremic Syndrome (aHUS)

aHUS is a severe and life-threatening, ultra-rare genetic disease characterized by chronic uncontrolled complement activation and thrombotic microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body, causing a reduction in platelet count (thrombocytopenia) and life-threatening damage to the kidney, brain, heart and other vital

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organs. Soliris is approved for the treatment of pediatric and adult patients with aHUS in the U.S., Europe and Japan. We are sponsoring a multinational registry to gather information regarding the natural history of patients with aHUS and the longer term outcomes during Soliris treatment. In addition, the FDA and European Commission (EC) have granted Soliris orphan drug designation for the treatment of patients with aHUS.

Strensiq (asfotase alfa)

Hypophosphatasia (HPP)

HPP is an ultra-rare genetic and progressive metabolic disease in which patients experience devastating effects on multiple systems of the body, leading to debilitating or life-threatening complications. HPP is characterized by defective bone mineralization that can lead to deformity of bones and other skeletal abnormalities, as well as systemic complications such as profound muscle weakness, seizures, pain, and respiratory failure leading to premature death in infants.

Strensiq, a targeted enzyme replacement therapy, is the first and only approved therapy for patients with HPP, and is designed to directly address underlying causes of HPP by aiming to restore the genetically defective metabolic process, thereby preventing or reversing the severe and potentially life-threatening complications in patients with HPP. In 2015, the FDA approved Strensiq for patients with perinatal-, infantile- and juvenile-onset HPP, the EC granted marketing authorization for Strensiq for the treatment of patients with pediatric-onset HPP, and Japan's Ministry of Health Labour and Welfare (MHLW) approved Strensiq for the treatment of patients with HPP. We are sponsoring a multinational registry to gather information regarding the natural history of patients with HPP and the longer-term outcomes during Strensiq treatment.

Kanuma (sebelipase alfa)

Lysosomal Acid Lipase Deficiency (LAL Deficiency or LAL-D)

LAL-D is a serious, life-threatening ultra-rare disease associated with premature mortality and significant morbidity. LAL-D is a chronic disease in which genetic mutations result in decreased activity of the LAL enzyme that leads to marked accumulation of lipids in vital organs, blood vessels, and other tissues, resulting in progressive and systemic organ damage including hepatic fibrosis, cirrhosis, liver failure, accelerated atherosclerosis, cardiovascular disease, and other devastating consequences.

Kanuma, a recombinant form of the human LAL enzyme, is the only enzyme-replacement therapy that is approved for the treatment for patients with LAL-D. In 2015, the FDA approved Kanuma for the treatment of patients with LAL-D and the EC granted marketing authorization of Kanuma for long-term enzyme replacement therapy in patients of all ages with LAL-D. On March 28, 2016, we announced that the MHLW approved Kanuma for the treatment of patients of all ages in Japan with LAL-D. We are sponsoring a multinational registry to gather information regarding the natural history of patients with LAL-D and the longer term outcomes during Kanuma treatment.

Clinical Development Programs

Our programs, including investigator sponsored clinical programs, include the following:

Product	Development Area	Indication	Development Stage
Soliris (eculizumab)	Neurology	Refractory Generalized Myasthenia Gravis (gMG)	Phase III
		Relapsing Neuromyelitis Optica Spectrum Disorder (NMOSD)	Phase III
	Transplant	Antibody Mediated Rejection (AMR) Presensitized Renal Transplant - Deceased Donor	Phase II
cPMP (ALXN1101)	Metabolic Disorders	Molybdenum Cofactor Deficiency (MoCD)Type A	Phase II / III
SBC-103	Metabolic Disorders	Mucopolysaccharidoses IIIB (MPS IIIB)	Phase I / II
ALXN1210 (IV)	Next Generation Complement Inhibitor	Paroxysmal Nocturnal Hemoglobinuria (PNH)	Phase III
		Atypical Hemolytic Uremic Syndrome (aHUS)	Phase III
ALXN1210 (Subcutaneous)	Next Generation Complement Inhibitor		Phase I

Soliris (eculizumab)

Neurology

Refractory Generalized Myasthenia Gravis (gMG)

Refractory gMG is an ultra-rare segment of Myasthenia Gravis, a debilitating, complement-mediated neuromuscular disease in which patients suffer profound muscle weakness throughout the body, resulting in slurred speech, impaired swallowing and choking, double vision, upper and lower extremity weakness, disabling fatigue, shortness of breath due to respiratory muscle weakness and episodes of respiratory failure. The FDA, EC and MHLW have granted orphan drug designation for eculizumab as a treatment for patients with refractory gMG.

In June 2016, we announced topline results of the Phase III REGAIN trial of eculizumab for the treatment of refractory gMG. The primary efficacy endpoint of change from baseline in Myasthenia Gravis-Activities of Daily Living Profile (MG-ADL) total score, a patient-reported assessment, at week 26, did not reach statistical significance (p=0.0698) as measured by a worst-rank analysis. The totality of data reviewed to date, including the first three secondary endpoints and a series of prospectively defined sensitivity analyses, shows early and sustained substantial improvements over 26 weeks for patients treated with eculizumab compared to placebo. The safety of eculizumab in this study was consistent with the Soliris labels. Additional data from the Phase III study was presented in July 2016. The data showed that 18 of 22 pre-defined endpoints and pre-specified analyses in the study, based on the primary and five secondary endpoints, achieved p-values below 0.05.

In January 2017, we announced that we filed for regulatory approval for eculizumab in refractory gMG in both the U.S. and Europe. These marketing applications were based on the comprehensive data from the Phase III REGAIN trial.

Relapsing Neuromyelitis Optica Spectrum Disorder (NMOSD)

Relapsing NMOSD is a severe and ultra-rare autoimmune disease of the central nervous system (CNS) that primarily affects the optic nerves and spinal cord. The disease leads to severe weakness, paralysis, respiratory failure, loss of bowel and bladder function, blindness and premature death. Enrollment and dosing are ongoing in a global, randomized, double-blind, placebo-controlled trial to evaluate eculizumab as a treatment for patients with relapsing NMOSD. The FDA, EC, and MHLW have each granted orphan designation for eculizumab as a treatment for patients with relapsing NMOSD.

Transplant

Antibody Mediated Rejection (AMR) in Presensitized Kidney Transplant Patients

AMR is the term used to describe a type of transplant rejection that occurs when the recipient has antibodies to the donor organ. Enrollment in a multi-national, multi-center controlled clinical trial of eculizumab in presensitized kidney transplant patients at elevated risk for AMR who received kidneys from deceased organ donors was completed in March 2013 and patient follow-up in the trial is continuing. In September 2013, researchers presented positive preliminary data from the eculizumab deceased-donor AMR kidney transplant study. In May 2015, new data from the Phase II single-arm deceased-donor transplant trial of eculizumab in prevention of acute AMR was presented and was consistent with previous positive reports.

cPMP (ALXN1101)

Molybdenum Cofactor Deficiency (MoCD) Disease Type A (MoCD Type A)

MoCD Type A is an ultra-rare metabolic disorder characterized by severe and rapidly progressive neurologic damage and death in newborns. MoCD Type A results from a genetic deficiency in cyclic Pyranopterin Monophosphate (cPMP), a molecule that enables the function of certain enzymes and the absence of which allows neurotoxic sulfite to accumulate in the brain. To date, there is no approved therapy available for MoCD Type A. There has been some early clinical experience with the recombinant cPMP replacement therapy in a small number of children with MoCD Type A, and we have completed enrollment in a natural history study in patients with MoCD Type A. cPMP received Breakthrough Therapy Designation from the FDA for the treatment of patients with MoCD Type A. Evaluation of our synthetic form of cPMP replacement therapy in a Phase I healthy volunteer study is complete. In addition, we completed enrollment in a multi-center, multinational open-label clinical trial of synthetic cPMP in patients with MoCD Type A switched from treatment with recombinant cPMP. Enrollment is ongoing in the Phase II/III pivotal open-label, single-arm trial of ALXN1101 for treatment-naïve neonates with MoCD Type A.

SBC-103

Mucopolysaccharidosis IIIB (MPS IIIB)

MPS IIIB is an ultra-rare, devastating and life-threatening disease which typically presents in children during the first few years of life. Genetic mutations result in decreased activity of the alpha-N-acetyl-glucosaminidase (NAGLU) enzyme, which leads to a buildup of abnormal amounts of heparan sulfate (HS) in the brain and throughout the body. Over time, this unrelenting systemic accumulation of HS causes progressive and severe cognitive decline, behavioral problems, speech loss, increasing loss of mobility, and premature death. Current treatments are palliative for the behavioral problems, sleep disturbances, seizures, and other complications, and these treatments do not address the root cause of MPS IIIB or stop disease progression.

SBC-103, a recombinant form of natural human NAGLU is designed to replace the missing (or deficient) NAGLU enzyme. SBC-103 was granted orphan drug designation by the FDA and by the EC. It received Fast Track designation by the FDA. The first-in-human trial of patients with MPS IIIB is ongoing. In March 2016, researchers presented 24-week results from this study that showed a 26.2 percent mean reduction in heparan sulfate in cerebrospinal fluid at the highest dose studied (3mg/kg every other week) in a Phase I/II study at six months. In July 2016, researchers presented preliminary results on brain MRI and neurocognitive assessments performed after 24 weeks of dosing suggesting preliminary evidence of potential for dose-dependent disease stabilization in patients treated with 0.3, 1, or 3mg/kg every other week of doses of SBC-103. Planned dose escalation of SBC-103 is now ongoing in this trial. In February 2017, the Board of Directors of Alexion made the decision to reduce our investment in SBC-103. The current Phase I/II clinical trial will not be expanded and no new patients will be added to the trial. Patients currently enrolled in the trial will continue to receive therapy.

ALXN1210

ALXN1210 is a highly innovative, longer-acting anti-C5 antibody discovered and developed by Alexion that inhibits terminal complement. In early studies, ALXN1210 demonstrated rapid, complete, and sustained reduction of free C5 levels. Alexion has completed enrollment in two ongoing clinical studies of ALXN1210 in patients with PNH-a Phase 1/2 dose-escalating study and an open-label, multi-dose Phase II study that is also evaluating longer dosing intervals beyond 8 weeks.

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Paroxysmal Nocturnal Hemoglobinuria (PNH)

In June 2016, we announced interim data from a Phase I/II study in patients with PNH showing that once-monthly dosing of ALXN1210 achieved rapid and sustained reductions in hemolysis, as measured by mean levels of lactate dehydrogenase (LDH), in 100 percent of treated patients. Chronic hemolysis in patients with PNH may be associated with life-threatening thromboses, recurrent pain, kidney disease, disabling fatigue, impaired quality of life, severe anemia, pulmonary hypertension, shortness of breath and intermittent episodes of dark-colored urine (hemoglobinuria). Researchers also reported that, at the time of analysis, 80 percent of patients who required at least 1 blood transfusion in the 12 months prior to treatment with ALXN1210 did not require transfusions while on treatment with ALXN1210. Furthermore, in December 2016, we reported new data from this same ongoing study that showed rapid and sustained reductions LDH in patients with PNH treated with once-monthly dosing. Patients also had improvements in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score from baseline, with patients in the higher-dose cohort achieving a two-fold greater improvement compared with the lower-dose cohort. In addition, we have completed enrollment and treatment is ongoing in an open-label, multi-dose Phase II study of ALXN1210 in patients with PNH designed to measure reductions in hemolysis and safety in several dosing cohorts and intervals evaluating monthly and longer dosing intervals. We have initiated a Phase III open-label, multinational, active-controlled study of ALXN1210 compared to eculizumab (Soliris) in adult patients with PNH who have never been treated with a complement inhibitor. The study is evaluating ALXN1210 administered intravenously every eight weeks. Patient enrollment is ongoing in this trial.

In June 2016 and January 2017, the EC and the FDA, respectively, granted orphan drug designation to ALXN1210, for the treatment of patients with PNH.

Atypical Hemolytic Uremic Syndrome (aHUS)

We initiated a Phase III open-label, single arm, multicenter study of ALXN1210 in adolescent and adult patients with aHUS who have never been treated with a complement inhibitor. In patients with aHUS, complement-mediated TMA leads to life-threatening damage to the kidney, brain, heart and other vital organs. The study will evaluate ALXN1210 administered intravenously every eight weeks. Patient recruitment will initiate in 2017 on this trial.

Subcutaneous (SC) Delivery

We have completed enrollment in a Phase I study in healthy volunteers to evaluate ALXN1210 delivered subcutaneously.

Manufacturing

We currently rely on internal manufacturing facilities and third party contract manufacturers, including Lonza Group AG and its affiliates (Lonza), to supply clinical and commercial quantities of our commercial products and product candidates. Our internal manufacturing facilities include our Ireland manufacturing facilities, our Rhode Island manufacturing facility (ARIMF), and facilities in Massachusetts and Georgia. We also utilize third party contract manufacturers for other manufacturing services including purification, product filling, finishing, packaging, and labeling.

We have various agreements with Lonza through 2028, with remaining total non-cancellable commitments of approximately $1,148. If we terminate certain supply agreements with Lonza without cause, we will be required to pay for product scheduled for manufacture under our arrangements. Under an existing arrangement with Lonza, we also pay Lonza a royalty on sales of Soliris manufactured at ARIMF and a payment with respect to sales of Soliris manufactured at Lonza facilities. During 2015, we entered into a new supply agreement with Lonza whereby Lonza will construct a new manufacturing facility dedicated to Alexion manufacturing at one of its existing facilities.

In addition, we have non-cancellable commitments of approximately $27 through 2019 with other third party manufacturers.

In March 2013, we received a Warning Letter (Warning Letter) from the FDA regarding compliance with current Good Manufacturing Practices (cGMP) at ARIMF. The Warning Letter followed receipt of a Form 483 Inspectional Observations by the FDA in connection with an FDA inspection that concluded in August 2012. The observations relate to commercial and clinical manufacture of Soliris at ARIMF. We responded to the Warning Letter in a letter to the FDA dated in April 2013. As previously disclosed, the FDA issued Form 483s in August 2014 and August 2015 relating to observations at ARIMF and the inspectional observations from the August 2014 and 2015 Form 483s have since been closed out by the FDA. During July 2016, the FDA completed a routine inspection at ARIMF and have

since confirmed receipt of our responses to the inspectional observations included in the Form 483 received during that inspection. We continue to manufacture products, including Soliris, at ARIMF, and we anticipate that the supply of Soliris to patients will not be interrupted as a result of the inspectional observations. While the resolution of the issues raised in the Warning Letter is difficult to predict, we do not currently believe a

loss related to this matter is probable or that the potential magnitude of such loss or range of loss, if any, can be reasonably estimated.

In April 2014, we purchased a fill/finish facility in Athlone, Ireland. After regulatory approvals, the facility will become our first company-owned fill/finish facility for our commercial and clinical products. In July 2016, we announced plans to construct a new biologics manufacturing facility at this site, which is expected to be completed by 2018.

In May 2015, we announced plans to construct a new biologics manufacturing facility on our existing property in Dublin, Ireland, which is expected to be completed by 2020.

Sales and Marketing

We have established a commercial organization to support current and future sales of our products in the U.S., Europe, Japan, Asia Pacific countries, and other territories. Our sales force is small compared to that of other drugs with similar revenues; however, we believe that a relatively smaller sales force is appropriate to effectively market our products due to the incidence and prevalence of rare diseases. If we receive regulatory approval in new territories or for new products or indications, we may expand our own commercial organizations in such territories and market and sell our products through our own sales force in these territories. However, we evaluate each jurisdiction on a country-by-country basis, and, in certain territories, we promote our products in collaboration with marketing partners or rely on relationships with one or more companies with established distribution systems and direct sales forces in certain countries.

Customers

Our customers are primarily comprised of distributors, pharmacies, hospitals, hospital buying groups, and other healthcare providers. In some cases, we may also sell our products to governments and government agencies. During 2016 and 2015, sales to our largest customer accounted for 16% and 18% respectively, of net product sales. Because of factors such as the pricing of our products, the limited number of patients, the short period from product sale to patient use and the lack of contractual return rights, customers often carry limited inventory. We also monitor inventory within our sales channels to determine whether deferrals are appropriate based on factors such as inventory levels compared to demand, contractual terms, financial strength of distributors and our ability to estimate returns. Please also see “Management’s Discussion and Analysis – Net Product Sales,” and Note 18 of the Consolidated Financial Statements included in this Annual Report on Form 10-K, for financial information about geographic areas.

Intellectual Property Rights and Market Exclusivity

Patents and other intellectual property rights are important to our business. We own or license a number of patents in the U.S. and foreign countries that cover our products and investigational compounds. We also file and prosecute patent applications covering new technologies and inventions that are meaningful to our business. In addition to patents, we rely on trade secrets, know-how, trademarks, regulatory exclusivity and other forms of intellectual property. Our intellectual property rights have material value and we act to protect them.

In the biopharmaceutical industry, two forms of intellectual property generally determine the period of a product’s market exclusivity: patent rights and regulatory forms of exclusivity. During the period of market exclusivity an innovative product generally realizes most of its commercial value.

Patents provide the owner with a right to exclude others from practicing an invention. In our business, patents may cover the active ingredients, uses, formulations, doses, administrations, delivery mechanisms, manufacturing processes and other aspects of a product. The period of patent protection for any given product may depend on the expiration date of various patents and may differ from country to country according to the type of patents, the scope of coverage and the remedies for infringement available in a country.

Most of our products and investigational compounds are protected by patents with varying terms that depend on the type of patent and its filing date. However, a significant portion of a product’s patent life can elapse during the time it takes to develop and obtain regulatory approval of the product. As compensation for such delay certain countries will extend a patent’s term, subject to a number of factors and caps.

Regulatory forms of exclusivity are another source of valuable rights that can contribute toward market exclusivity for an innovative biopharmaceutical product. Many developed countries provide such non-patent incentives to develop medicines. In the U.S., Europe and Japan, for instance, regulatory intellectual property rights provide incentives to develop medicines for rare diseases, or orphan drugs, and medicines for pediatric patients. Those countries and others

also provide data protection for a

period of time after the approval of a new drug, during which regulatory agencies may not rely on the innovator's data to approve a biosimilar or generic copy. Regulatory forms of exclusivity can work in conjunction with patents to strengthen market exclusivity, and in countries where patent protection has expired or does not exist, regulatory forms of exclusivity can extend a product's market exclusivity period.

Soliris Exclusivity

With respect to Soliris, we own an issued U.S. patent that covers the eculizumab composition of matter and will expire in 2021, taking into account patent term extension. Soliris is also protected in the U.S. by regulatory data exclusivity until 2019 and by orphan drug exclusivity for treating aHUS until 2018. In Europe we have supplementary protection certificates that extend rights associated with a composition of matter patent until 2020 in certain countries. Soliris is also protected in Europe by orphan drug exclusivity until 2019 for PNH and until 2023 for aHUS. In addition to the foregoing patent and regulatory protections, we own other patents and pending patent applications that are directed to various aspects of eculizumab and which may provide additional protection for Soliris.

Strensiq Exclusivity

With respect to Strensiq, we own an issued U.S. patent that covers the asfotase alfa composition of matter and will expire in 2026. We have applied for an extension of the U.S. patent term. Strensiq is also protected in the U.S. by orphan drug exclusivity until 2022 and by regulatory data exclusivity until 2027. In Europe, we own two issued patents that cover the asfotase alfa composition of matter and will expire in 2025 and 2028. We have applied for supplementary protection certificates in the European countries. Strensiq is also protected in Europe by orphan drug exclusivity and regulatory data exclusivity until 2025. In other countries we own corresponding patents that will expire between 2025 and 2028, not including possible extensions.

Kanuma Exclusivity

With respect to Kanuma, we own issued patents in the U.S., Europe and other countries that cover methods of using the product to treat LAL-D and will expire in 2031. The European patent is under challenge in an administrative opposition proceeding. An exclusively licensed composition of matter patent also protects Kanuma in certain European countries until it expires in 2021, though we also applied for supplementary protection certificates in those countries. In the U.S. Kanuma also is protected by orphan drug exclusivity until 2022 and by regulatory data exclusivity until 2027. In Europe it is protected by orphan drug exclusivity and regulatory data exclusivity until 2025.

Soliris, Strensiq, and Kanuma Regulatory Protection

As noted above, for each of Soliris, Strensiq and Kanuma we rely on regulatory forms of exclusivity such as data protection and orphan drug protection to support the product's market exclusivity. Specific aspects of the laws governing regulatory exclusivity vary by country, but most forms of regulatory exclusivity do not prevent competitive products from gaining regulatory approval on the basis of the competitor's own safety and efficacy data, even when the competitive product is a biosimilar or generic copy. In certain countries, however, orphan drugs can obtain a period of exclusivity during which no competitive product containing the same drug may be approved for the same orphan indication.

We also own U.S. and foreign patents and patent applications that protect our investigational compounds and product candidates. At present, it is not known whether any such investigational compound or product candidate will be approved for human use and sale.

License and Collaboration Agreements

From time to time, we enter into arrangements with third parties, including collaboration and licensing arrangements, for the development, manufacture and commercialization of products and product candidates. These strategic alliances are intended to strengthen and advance our R&D capabilities and diversify our product pipeline to support the growth of our marketed product base. The arrangements, which generally provide Alexion with rights to specialized technology and intellectual property for the development of potential product candidates, often require non-refundable, upfront license fees, development, regulatory and commercial milestones, as well as royalty payments on commercial sales.

Government Regulation

Drug Development and Approval in the United States

The preclinical studies and clinical testing, manufacture, labeling, storage, record keeping, advertising, promotion, export, and marketing, among other things, of our products and product candidates , including Soliris, Strensiq and Kanuma, are subject to extensive regulation by governmental authorities in the US, the European Union (EU) and other territories. In the U.S., pharmaceutical products are regulated by the FDA under the Federal Food, Drug, and Cosmetic Act and other laws, including, in the case of biologics, the Public Health Service Act. Our three approved products are regulated by the FDA as biologics. Biologics require the submission of a Biologics License Application (BLA) and approval by the FDA prior to being marketed in the U.S. In the case of Kanuma, which is derived from egg whites from select hens, we also submitted a New Animal Drug Application (NADA) for approval by the FDA. Manufacturers of biologics and drugs derived from animal origin may also be subject to state regulation. Failure to comply with FDA requirements, both before and after product approval, may subject us and/or our partners, contract manufacturers, and suppliers to administrative or judicial sanctions, including FDA refusal to approve applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, fines and/or criminal prosecution.

The process for obtaining regulatory approval to market a biologic is expensive, often takes many years, and can vary substantially based on the type, complexity, and novelty of the product candidates involved. The steps required before a biologic may be approved for marketing of an indication in the U.S. generally include:

(1) preclinical laboratory tests and animal tests;

(2) submission to the FDA of an investigational new drug (IND) application for human clinical testing, which must become effective before human clinical trials may commence;

(3) adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for its intended use;

(4) submission to the FDA of a BLA or supplemental BLA;

(5) FDA pre-approval inspection of the manufacturing sites identified in the BLA; and

(6) FDA review and approval of the BLA or supplemental BLA.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as toxicological and pharmacological animal studies to assess the potential safety and efficacy of the product candidate. Preclinical safety tests intended for submission to FDA must be conducted in compliance with FDA's Good Laboratory Practice (GLP) regulations and the U.S. Department of Agriculture's Animal Welfare Act. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application which must become effective before human clinical trials may be commenced. The IND will automatically become effective 30 days after receipt by the FDA, unless the FDA before that time raises concerns about the drug candidate or the conduct of the trials as outlined in the IND. The IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. We cannot assure you that submission of an IND will result in FDA authorization to commence clinical trials or that once commenced, other concerns will not arise. FDA may stop the clinical trials by placing them on "clinical hold" because of concerns about the safety of the product being tested, or for other reasons. Clinical trials involve the administration of the investigational product to healthy volunteers or to patients, under the supervision of qualified principal investigators. The conduct of clinical trials is subject to extensive regulation, including compliance with the FDA's bioresearch monitoring regulations and Good Clinical Practice (GCP) requirements, which establish standards for conducting, recording data from, and reporting the results of clinical trials, and are intended to assure that the data and reported results are credible and accurate, and that the rights, safety, and well-being of study participants are protected. Clinical trials must be conducted in accordance with protocols that detail the objectives of the study, the criteria for determining subject eligibility, the dosing plan, patient monitoring requirements, timely reporting of adverse events, and other elements necessary to ensure patient safety, and any efficacy criteria to be evaluated. Each protocol must be submitted to FDA as part of the IND; further, each clinical study at each clinical site must be reviewed and approved by an independent institutional review board, prior to the recruitment of subjects. The institutional review board's role is to protect the rights and welfare of human subjects involved in clinical studies by evaluating, among other things, the potential risks and benefits to subjects, processes for obtaining informed consent, monitoring of data to ensure subject safety, and provisions to protect the subjects'

privacy. Foreign studies conducted under an IND application must meet the same requirements that apply to studies being conducted in the U.S. Data from a foreign study not conducted under an IND may be submitted in support of a BLA if the study was conducted in accordance with GCP and FDA is able to validate the data.