ALEXION PHARMACEUTICALS INC
Form 10-K
February 19, 2013

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, 2012
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.)

352 Knotter Drive, Cheshire Connecticut 06410
(Address of Principal Executive Offices) (Zip Code)
203-272-2596
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:	Common Stock, par value $0.0001
	Rights to Purchase Junior Participating
	Cumulative Preferred 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 x 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 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, 2012, was $18,920,399,568.(1)

The number of shares of Common Stock outstanding as of February 11, 2013 was 195,209,249.

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 06, 2013, are incorporated by reference into Part III of this report.

(1) Excludes 2,231,014 shares of common stock held by directors and executive officers at June 30, 2012. 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.

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 our management's current expectations, estimates and projections about our industry 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® (eculizumab) for its approved indications and any expanded uses, timing and effect of sales of Soliris in various markets worldwide, pricing for Soliris, level of insurance coverage and reimbursement for Soliris, level of future Soliris sales and collections, timing regarding development and regulatory approvals for additional indications or in additional territories for Soliris, the medical and commercial potential of additional indications for Soliris, 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 commercial infrastructure and interest about Soliris and our drug candidates in the patient, physician and payer communities, the safety and efficacy of Soliris and our product candidates, estimates of the potential markets and estimated commercialization dates for Soliris and our drug candidates around the world, sales and marketing plans, any changes in the current or anticipated market demand or medical need for Soliris or our drug candidates, status of our ongoing clinical trials for eculizumab, asfotase alfa and our other product candidates, commencement dates for new clinical trials, clinical trial results, evaluation of our clinical trial results by regulatory agencies, prospects for regulatory approval, 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 companies and programs, 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 Soliris infringes their intellectual property, estimates of the capacity of manufacturing and other facilities to support Soliris 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, assessment of impact of recent accounting pronouncements, declines in sovereign credit ratings or sovereign defaults in countries where we sell Soliris, delay of collection or reduction in reimbursement due to adverse economic conditions or changes in government and private insurer regulations and approaches to reimbursement, 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 Securities and Exchange Commission.

Item 1. BUSINESS.

(dollars and shares in thousands)

Overview

We are a biopharmaceutical company focused on serving patients with severe and ultra-rare disorders through the innovation, development and commercialization of life-transforming therapeutic products. Our marketed product Soliris® (eculizumab) is the first and only therapeutic approved for patients with two severe and ultra-rare disorders resulting from chronic uncontrolled activation of the complement component of the immune system: paroxysmal

nocturnal hemoglobinuria (PNH), a life-threatening and ultra-rare genetic blood disorder, and atypical hemolytic uremic syndrome (aHUS), a life-threatening and ultra-rare genetic disease. We are also evaluating additional potential indications for Soliris in severe and ultra-rare diseases in which chronic uncontrolled complement activation is the underlying mechanism, and we are progressing in various stages of development with additional biotechnology product candidates as treatments for patients with severe and ultra-rare disorders. We were incorporated in 1992 and began commercial sale of Soliris in 2007.

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 the therapeutic areas of hematology, nephrology, transplant rejection and neurology. 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. PNH is an ultra-rare, debilitating and life-threatening, genetic deficiency 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).

Soliris was approved for the treatment of PNH by the U.S. Food and Drug Administration (FDA) and the European Commission (EC) in 2007 and by Japan's Ministry of Health, Labour and Welfare (MHLW) in 2010, and has been approved in several other territories. Additionally, Soliris has been granted orphan drug designation for the treatment of PNH in the United States, Europe, Japan and several other territories.

In September 2011, Soliris was approved by the FDA for the treatment of pediatric and adult patients with aHUS. aHUS is a genetic ultra-rare disease characterized by chronic uncontrolled complement activation and thrombotic microangiopathy, 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 organs. Also, in November 2011, the EC granted marketing authorization for Soliris to treat pediatric and adult patients with aHUS in Europe. The FDA and EC have granted Soliris orphan drug designation for the treatment of patients with aHUS.

Significant Developments

Enobia Acquisition

On February 7, 2012, we acquired Enobia Pharma Corp. (Enobia), a privately held clinical-stage biotechnology company based in Montreal, Canada and Cambridge, Massachusetts, in a transaction accounted for under the acquisition method of accounting for business combinations. Enobia's lead product candidate, asfotase alfa, is a human recombinant targeted alkaline phosphatase enzyme-replacement therapy for patients suffering with hypophosphatasia (HPP), an ultra-rare, life-threatening, genetic metabolic disease for which there are no approved treatments. We agreed to make an upfront payment of $610,000 subject to purchase price adjustments, which resulted in us making a cash payment of $623,876 for 100% of Enobia's capital stock. Additional contingent payments of up to an aggregate of $470,000 may be due upon reaching various regulatory and sales milestones. We financed the acquisition with a combination of existing cash and proceeds from our credit facility.

Credit Facilities

On February 7, 2012, we and our wholly-owned Swiss subsidiary, Alexion Pharma International Sàrl, entered into a Credit Agreement (Credit Agreement) with the lenders party thereto, Bank of America, N.A., as administrative agent, Merrill Lynch, Pierce, Fenner & Smith Incorporated and J.P. Morgan Securities LLC, as joint lead arrangers and joint book managers, JPMorgan Chase Bank, N.A., as syndication agent and RBS Citizens, National Association and Suntrust Bank as co-documentation agents. The Credit Agreement provides for a $240,000 senior secured term loan facility and a $200,000 senior secured revolving credit facility, which includes up to a $60,000 sublimit for letters of credit and a $10,000 sublimit for swingline loans. Alexion used the facilities to pay a portion of the consideration for the acquisition of Enobia. The facilities can also be used for working capital requirements, acquisitions and other general corporate purposes. Simultaneously with entering into the Credit Agreement, we terminated our Second Amended and Restated Credit Agreement, dated March 7, 2011.

Common Stock Offering

In May 2012, in conjunction with our addition into the S&P 500 Index, we completed the sale of 5,000 shares of our common stock in a public offering. The net proceeds from the sale of shares in the offering were $462,212.

Products and Development Programs

The human immune system defends the body from attack or invasion by infectious agents or pathogens. This is accomplished through a complex system of proteins and cells, primarily complement proteins, antibodies and white blood cells, each with a specialized function. Under normal circumstances, complement proteins, together with antibodies and white blood cells, act to protect the body by removing:

- harmful micro-organisms;
- cells containing foreign proteins known as antigens; and
- potential disease-causing combinations of antigens and antibodies known as immune complexes.

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When activated by certain stimuli, the immune system triggers a series of enzymatic and biochemical reactions called the complement cascade that results in an inflammatory response. This inflammatory response is one of the immune system's weapons against foreign pathogens or otherwise diseased tissue. However, under certain circumstances, the complement cascade may cause excessive or inappropriate activation, and/or an individual may be deficient in naturally occurring complement inhibitors, all of which may result in acute and chronic inflammatory conditions and damage to healthy tissues.

We focus our product development programs on life transforming therapeutics for diseases for which we believe current treatments are either non-existent or inadequate. Eculizumab is a humanized antibody known as a C5 terminal complement inhibitor (C5 Inhibitor), which is designed to selectively block the production of inflammation-causing proteins of the complement cascade. We believe that selective suppression of this immune response may provide a significant therapeutic advantage relative to existing therapies. In addition to PNH and aHUS, for which the use of eculizumab has been approved in the United States and Europe, we believe that C5 Inhibitors may be useful in the treatment of a variety of other serious diseases and conditions resulting from uncontrolled complement activation. Our programs, including investigator sponsored clinical programs, include the following:

Product	Development Area	Indication	Development Stage
Soliris (eculizumab)	Hematology	Paroxysmal Nocturnal Hemoglobinuria (PNH)	Commercial
		PNH Registry	Phase IV
		PNH Pediatric Trial	Phase II
		Cold Agglutinin Disease (CAD)*	Phase II
	Hematology/Nephrology	Atypical Hemolytic Uremic Syndrome (aHUS)	Commercial
		aHUS Trials	Phase IV
		aHUS Registry	Phase IV
	Nephrology	STEC-HUS (Shiga-toxin producing E. Coli Hemolytic Uremic Syndrome)	Phase II
		MPGN II/C3 Nephropathy*	Phase II
		Presensitized Renal Transplant - Living Donor	Phase II
		Presensitized Renal Transplant - Deceased Donor	Phase II
		Delayed Kidney Transplant Graft Function*	Phase II
		ABO Incompatible Renal Transplant*	Phase II
	Neurology	Neuromyelitis Optica (NMO)*	Phase II
		Myasthenia Gravis (MG)	Phase II
Asfotase alfa	Metabolic Disorders	Hypophosphatasia (HPP)	Phase II
cPMP	Metabolic Disorders	MoCD Type A	Preclinical
ALXN 1102/1103	Hematology	PNH	Phase I
ALXN 1007	Inflammatory Disorders		Phase I

*Investigator Initiated Trial

Our most advanced programs focus on two therapeutic areas: hematology and nephrology. We are also advancing our pipeline programs with a focus primarily on neurology and metabolic disorders.

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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 the therapeutic areas of hematology, nephrology including transplant rejection, and neurology. Soliris is a humanized antibody which, administered at the doses currently prescribed, generally blocks complement activity for one to two weeks after a single dose.

Soliris was approved for the treatment of PNH by the FDA and the EC in 2007, by Japan's MHLW in 2010 and has been approved in several other territories. Additionally, Soliris was granted orphan drug designation for the treatment of PNH in the United States, Europe, Japan and several other territories.

Soliris was approved for the treatment of aHUS by the FDA and the EC in 2011. Soliris was granted orphan drug designation for the treatment of aHUS in the United States and Europe.

Orphan drug designation generally entitles us to exclusivity for certain periods of time, subject to limited circumstances. However, if a competitive product that is the same as Soliris, as defined under the applicable regulations, is shown to be clinically superior to our product in the treatment of PNH, or if a competitive product is different from Soliris, as defined under the applicable regulations, the orphan drug exclusivity we have obtained may not restrict the approval of such competitive product.

Hematology

Paroxysmal Nocturnal Hemoglobinuria (PNH)

PNH is an ultra-rare, debilitating and life-threatening blood disorder in which an acquired genetic deficiency causes uncontrolled complement activation which leads to life-threatening complications. Patients with PNH have an acquired genetic deficiency in certain protective proteins on the surface of their blood cells, allowing their own complement system to attack and destroy these blood cells. Patients with PNH suffer from chronic complement activation of some of their blood cells and also hemolysis, or destruction of red blood cells caused by the C5 cleavage product C5b-9. This hemolysis is believed to lead to further clinical complications including thromboses, kidney disease, liver dysfunction, disabling fatigue, impaired quality of life, recurrent pain, shortness of breath, pulmonary hypertension, intermittent episodes of dark colored urine (hemoglobinuria), and anemia. Approximately one-half of the patients with PNH die from the disease within 10 to 15 years of diagnosis.

Our marketed product Soliris is the first and only therapy approved for the treatment of patients with PNH. We continue to work with researchers to expand the base of knowledge in PNH and the utility of Soliris to treat patients with PNH. Additionally, we are sponsoring multinational registries to gather information regarding the natural history of patients with PNH and the longer term outcomes during Soliris treatment.

Cold Agglutinin Disease (CAD)

We are aware that dosing is ongoing in an investigator-initiated Phase II study of eculizumab in patients for the treatment of CAD. CAD is a severe, ultra-rare complement-mediated autoimmune disease characterized by the presence of high concentrations of circulating complement-activating antibodies directed against red blood cells. As observed with PNH patients, CAD patients also suffer from the clinical consequences of severe hemolysis.

As blood is cooled during circulation through the distal parts of the arms and legs, specific antibodies bind to the red blood cells resulting in activation of the complement cascade and red blood cell lysis. Clinical manifestations of CAD include symptoms of chronic hemolysis such as fatigue, dyspnea, weakness, hemoglobinuria, kidney damage, pallor and jaundice. In the most severe cases, complications of progressive hemolysis or anemia may result in death. Current therapies, including cold avoidance, corticosteroids, immunosuppressive drugs, intravenous immunoglobulin G and chemotherapy agents are largely ineffective in controlling hemolysis in patients with CAD.

Hematology/Nephrology

Atypical Hemolytic Uremic Syndrome (aHUS)

aHUS is a chronic and life-threatening ultra-rare genetic disease in which uncontrolled complement activation causes blood clots in small blood vessels throughout the body (thrombotic microangiopathy, or TMA) leading to kidney failure, stroke, heart attack and death. Our marketed product Soliris is the first and only therapy approved for the treatment of patients with aHUS.

In patients with aHUS, deficiency of naturally occurring complement inhibitors causes uncontrolled complement activation which leads to systemic 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 organs. The prognosis for patients with aHUS is generally poor. Approximately 70% of patients with the most common mutation experience chronic renal insufficiency, chronic dialysis, or death within one year after the first clinical manifestation of TMA. aHUS commonly recurs in patients who undergo renal transplantation and, depending upon the mutation, the disease can lead to loss of the transplanted kidney in up to approximately 90% of aHUS patients who undergo kidney transplantation.

Approximately 50% of patients diagnosed with aHUS have been identified to have genetic mutations in at least one of the complement control proteins or neutralizing autoantibodies to complement regulatory factors, which can lead to uncontrolled complement activation. Excessive complement activation may contribute to the blood vessel inflammation and clotting by stimulating activation of white blood cells, platelets and the endothelial lining of blood vessels.

As a post marketing requirement, we have now completed enrollment in a prospective open-label trial in adult aHUS and, separately, enrollment has been completed in a prospective pediatric aHUS study.

Nephrology

Shiga-toxin producing E. Coli Hemolytic Uremic Syndrome (STEC-HUS)

STEC-HUS is a life-threatening, complement-mediated ultra-rare disorder that results from exposure to Enterohemorrhagic E.Coli, (EHEC). Our STEC-HUS development program was initiated in connection with the widespread outbreak of EHEC in Germany in May and June 2011. Many EHEC patients rapidly progressed to STEC-HUS during this outbreak. As in several other conditions with severe and uncontrolled complement activation, including aHUS, complement activation in STEC-HUS results in TMA. Although aHUS and STEC-HUS exhibit similar life-threatening TMA manifestations, aHUS and STEC-HUS are different disorders. aHUS is a chronic genetic disease of uncontrolled complement activation, while STEC-HUS is not genetic and follows an isolated episode of infection. STEC-HUS is an ultra-rare disorder, comprising only a small sub-set of the already rare population of patients with EHEC. Following an authorization by the Paul-Ehrlich-Institut, Germany's health care regulatory body for biologics, and an access program for patients initiated in May 2011, we initiated an open-label clinical trial to investigate eculizumab as a treatment for patients with STEC-HUS. Enrollment in this trial has been completed. The FDA and the EC have each granted orphan designation for eculizumab as a treatment for patients with STEC-HUS.

MPGN II/C3 Nephropathy

We are aware that independent investigators have completed enrollment in studies aimed at evaluating eculizumab in patients with membrano-proliferative glomerulonephritis (MPGN II or dense deposit disease) as well as patients with a similar disease referred to as C3 nephropathy. MGPN II and C3 nephropathy are ultra-rare forms of glomerulonephritis, associated with genetic mutations in complement inhibitor genes leading to sustained uncontrolled complement activation and inflammation. Clinically, this disease is characterized by the onset of severe proteinuria (excess protein in the urine), often accompanied by nephrotic syndrome which is refractory to immunosuppressant therapy. In most cases, the disease progresses to chronic renal failure, requiring dialysis and renal transplantation.

Acute Humoral Rejection (AHR) in Presensitized Kidney Transplant Patients

Patients undergoing solid organ transplantation may experience severe AHR in the early post-transplant period. For example, in a patient undergoing a kidney transplant this may be characterized by the acute onset of renal dysfunction and rapid progression to destruction of the transplanted kidney.

AHR results when antibodies in the transplant recipient vigorously attack the blood vessels of the donor kidney. During severe AHR, these donor specific antibodies bind to the blood vessel lining of the donor organ and initiate activation of the complement cascade, resulting in severe blood vessel inflammation and clotting. Administration of a C5 inhibitor in animal models of AHR inhibits complement activation, tissue damage and transplant rejection.

We initiated enrollment in a multi-national, multi-site controlled clinical trial of eculizumab in presensitized renal transplant patients at elevated risk for AHR who will receive living donor grafts, and we have initiated enrollment in a multi-national, multi-site controlled clinical trial of eculizumab in presensitized renal transplant patients at elevated risk for AHR who will receive deceased donor grafts. We are also aware that an independent investigator has started enrolling patients in a clinical trial to evaluate eculizumab in kidney transplant patients sensitized to their donor kidney due to an ABO blood group mismatch between donor and recipient.

Delayed Kidney Transplant Graft Function

We are aware that dosing is ongoing in an investigator-initiated Phase II study of eculizumab in patients at elevated risk for delayed graft function (DGF) following kidney transplant.

DGF is the term used to describe the failure of a kidney or other organs to function immediately after transplantation due to ischemia-reperfusion and immunological injury. After kidney transplantation, DGF can be considered a form of acute kidney injury post-transplantation and is an important complication of kidney transplantation. The frequency of DGF can be as high as 50% in some kidney transplant settings. DGF complicates post-transplant management, increases morbidity and prolongs patient hospitalization. In addition to the acute kidney injury, DGF predisposes the transplanted kidney to both acute and chronic rejection and increases the risk of chronic allograft nephropathy and premature graft loss. Studies have indicated that activation of the complement cascade may be a key early event required for the development of DGF following kidney transplant. There are currently no accepted or approved therapies for prevention or treatment of DGF following kidney transplantation.

Neurology

Neuromyelitis Optica (NMO)

NMO is a severe and ultra-rare autoimmune disease of the central nervous system (CNS) that primarily affects the optic nerves and spinal cord. Individuals with NMO develop optic neuritis, which causes pain in the eye and vision loss, and transverse myelitis, which causes weakness, numbness, and sometimes paralysis of the arms and legs, weakness or paralysis of respiratory muscles sometimes leading to respiratory failure, along with sensory disturbances and loss of bladder and bowel control.

Preliminary data from the investigator-initiated Phase II clinical trial of eculizumab in severe and relapsing NMO patients was presented to the American Neurological Association (ANA) meeting in October 2012. The study was reported to have achieved its primary efficacy endpoint with a high degree of clinical and statistical significance and several key secondary endpoints were also achieved.

Myasthenia Gravis (MG)

MG is an ultra-rare autoimmune syndrome characterized by complement activation leading to the failure of neuromuscular transmission. Patients with MG initially experience weakness in their ocular, or eye muscles, and the disease typically progresses to head, spinal, limb and respiratory muscles. Symptoms can include drooping eyelids, blurred vision, slurred speech, difficulty chewing or swallowing, weakness in the arms and legs and difficulty breathing. In an experimental animal model of MG, administration of a C5 Inhibitor was found to prevent experimentally acquired MG and to inhibit disease progression.

Preliminary data from a Phase II trial evaluating the safety and efficacy of eculizumab in patients with severe, refractory MG demonstrated an encouraging disease improvement signal and was presented at the Myasthenia Gravis Foundation Annual Meeting in September 2011. We continue to work with investigators to design the next clinical trial to evaluate eculizumab as a treatment for patients with severe and refractory MG.

Asfotase Alfa

Hypophosphatasia (HPP)

HPP is an ultra-rare, genetic, and life-threatening metabolic disease characterized by impaired phosphate and calcium regulation, leading to progressive damage to multiple vital organs including destruction and deformity of bones, profound muscle weakness, seizures, impaired renal function, and respiratory failure. The severe manifestations of the genetic deficiency in HPP affect people of all ages, and approximately 50% of infants with the disease do not survive past one year of age. HPP is caused by mutations in the gene encoding the enzyme Tissue Nonspecific Alkaline Phosphatase. This enzyme normally breaks

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down metabolic substrates such as inorganic pyrophosphate and pyridoxal phosphate.
Asfotase alfa, a targeted enzyme replacement therapy in Phase II clinical trials for patients with HPP, is designed to directly address the morbidities and mortality of HPP by targeting alkaline phosphatase directly to the deficient tissue. In this way, asfotase alfa is designed to normalize the genetically defective metabolic process and prevent or reverse the severe, crippling and life-threatening complications of dysregulated mineral metabolism in patients with HPP. Initial studies with asfotase alfa in HPP patients indicate that the treatment significantly decreases the levels of targeted metabolic substrates. We have initiated a natural history study in infants with HPP and are currently dosing patients in a separate global trial of severe infant HPP patients. We acquired asfotase alfa in February 2012 in connection with our acquisition of Enobia.

cPMP
Molybdenum Cofactor Deficiency (MoCD) Disease Type A (MoCD Type A)
MoCD Type A is a 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 production of certain enzymes, 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 cPMP replacement therapy in a small number of children with MoCD Type A. We are currently conducting pre-Investigational New Drug (IND) toxicology studies with cPMP replacement therapy.

ALXN 1102/1103
ALXN 1102/1103 is a novel alternative pathway complement inhibitor with a mechanism of action unique from Soliris. ALXN 1102 is currently being investigated in a Phase I single dose, dose escalating safety and pharmacology study. ALXN 1103 is being dosed in the same Phase I trial as a subcutaneous formulation.

ALXN 1007
ALXN 1007 is a novel humanized antibody designed to target rare and severe inflammatory disorders and is a product of our proprietary antibody discovery technologies. ALXN 1007 is currently being investigated in a Phase I single dose, dose escalating safety and pharmacology study in healthy volunteers.
Manufacturing
We currently rely on two manufacturing facilities, Alexion's Rhode Island manufacturing facility (ARIMF) and Lonza Group AG and its affiliates (Lonza), to produce commercial and clinical bulk quantities of Soliris, and we rely on Lonza for clinical quantities of asfotase alfa. We produce our clinical and preclinical quantities of our other product candidates at ARIMF. We also depend on a limited number of third party providers for other services with respect to our clinical and commercial requirements, including product finishing, packaging, vialing and labeling.
We have various agreements with Lonza, with remaining total commitments of approximately $169,000 through 2018. Such commitments may be canceled only in limited circumstances. If we terminate certain supply agreements with Lonza without cause, we will be required to pay for product scheduled for manufacture under our arrangement. Under an existing arrangement with Lonza, we also pay Lonza a royalty on sales of Soliris manufactured at ARIMF.
Sales and Marketing
We have established a commercial organization to support current and future sales of Soliris in the United States, in the major markets in European Union, Japan, Asia Pacific countries, and other territories. Our sales force for Soliris is small compared to that of other drugs with similar gross revenues; however, we believe that a relatively smaller sales force is appropriate to effectively market Soliris due to the limited PNH and aHUS patient populations. If we receive regulatory approval in new territories, we may expand our own commercial organizations in such territories and market and sell Soliris through our own sales force in these territories. However, we will evaluate each jurisdiction on a country-by-country basis, and it is possible that we will promote Soliris 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

In the United States, our customers are primarily specialty distributors and specialty pharmacies which supply physician office clinics, hospital outpatient clinics, infusion clinics or home health care providers. We also sell Soliris to government agencies. Outside the United States, our customers are primarily hospitals, hospital buying groups, pharmacies, other health care providers and distributors.

During 2012, sales to our two largest customers accounted for 21% and 12% of our Soliris net product sales. During 2011, sales to our two largest customers accounted for 19% and 12% of our Soliris net product sales.

Because of factors such as the pricing of Soliris, the limited number of patients, the short period from product sale to patient infusion and the lack of contractual return rights, Soliris customers generally carry limited inventory. We also monitor inventory within our sales channels to determine whether deferrals are appropriate based on factors such as inventory levels, contractual terms and financial strength of distributors.

Please also see "Management’s Discussion and Analysis – Net Product Sales," and Note 15 of the Consolidated Financial Statements included in this Annual Report on Form 10-K, for financial information about geographic areas.

Patents and Proprietary Rights

Patents and other proprietary rights are important to our business. Our practice is to file patent applications to protect technology, inventions and improvements to our technologies that are considered important to the development of our business. We also rely upon our trade secrets, know-how, and continuing technological innovations, as well as patents that we have licensed or may license from other parties, to develop and maintain our competitive position.

We have filed several U.S. patent applications and international counterparts of certain of these applications. In addition, we have in-licensed several additional U.S. and international patents and patent applications. As of December 31, 2012, we owned or in-licensed 89 U.S. patents and 45 U.S. patent applications. These patents and patent applications relate to technologies or products in the C5 Inhibitor program, high throughput screening, vectors, cancer, recombinant antibodies, bone delivery conjugates, natriuretic peptides, human molybdenum cofactor deficiency, targeted complement inhibitors, and other technologies. As of December 31, 2012, we owned or in-licensed 93 foreign patents and 370 pending foreign patent applications.

With respect to Soliris, we have an issued U.S. patent that will expire in 2021, taking into account patent term extension. In Europe, a corresponding issued patent covering Soliris expires in 2015 and, taking into account the Supplementary Protection Certificates (SPC) that we have filed for in various European countries, exclusivity for Soliris will extend into 2020 in those countries in which an SPC is granted. Patents covering Soliris in Japan and other countries expire between 2015 and 2020. We owe royalties and other fees to owners of one or more patents in connection with the manufacture and sale of Soliris for PNH and aHUS, and we may owe royalties and fees to other third parties with respect to any previous or future manufacture and sale of Soliris and our product candidates.

We also own U.S. and foreign patents and patent applications for our product candidates other than Soliris. At present, each such product candidate is in early stage development, and it is not known whether any such product candidate will ever be approved for human use and sale.

Our success will depend in part on our ability to obtain and maintain U.S. and international patent protection for our products and development programs, to preserve our trade secrets and proprietary rights, and to operate without infringing on the proprietary rights of third parties or having third parties circumvent our rights. Because of the length of time and expense associated with bringing new products through development and regulatory approval to the marketplace, the health care industry has traditionally placed considerable importance on obtaining patent and trade secret protection for significant new technologies, products and processes. Significant legal issues remain to be resolved as to the extent and scope of patent protection for biotechnology products and processes in the United States and other important markets outside of the United States. Accordingly, there can be no assurance that patent applications owned or licensed by us will issue as patents, or that any issued patents will afford meaningful protection against competitors. Moreover, once issued, patents are subject to challenge through both administrative and judicial proceedings in the United States and in foreign jurisdictions. Such proceedings include interference proceedings before the U.S. Patent and Trademark Office and opposition proceedings before the European Patent Office. Litigation may be required to enforce our intellectual property rights. Any litigation or administrative proceeding may result in a significant commitment of our resources and, depending on outcome, may adversely affect the validity and scope of certain of our patent or other proprietary rights.

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We are aware of broad patents owned by others relating to the manufacture, use and sale of recombinant humanized antibodies, recombinant human antibodies, and recombinant human single chain antibodies. Soliris and many of our product candidates are either genetically engineered antibodies, including recombinant humanized antibodies, recombinant human antibodies, or recombinant human single chain antibodies. We have received notices from the owners of patents claiming that their patents may be infringed by the development, manufacture or sale of Soliris or some of our drug candidates. For example, in January 2011, Novartis Vaccines & Diagnostics, Inc. (Novartis) filed a civil action in the U.S. District Court for the District of Delaware alleging that the manufacture of Soliris infringes their U.S. patent number 5,688,688. We are also aware of other patents owned by third parties that might be claimed by such third parties to be infringed by the development and commercialization of Soliris or some of our product candidates. In respect to some of these patents, we have obtained licenses, or expect to obtain licenses. However, with regard to such other patents, we have determined in our judgment that:

- our products do not infringe the patents;
- the patents are not valid; or
- we have identified and are testing various modifications that we believe should not infringe the patents and which should permit commercialization of our product candidates.

If any patent holder successfully challenges our judgment that our products do not infringe their patents or that their patents are invalid, we could be required to pay costly damages or to obtain a license to sell or develop our drugs. A required license may be costly or may not be available on acceptable terms, if at all. A costly license, or inability to obtain a necessary license, could materially and adversely affect our ability to commercialize our products, including Soliris.

On a quarterly basis, we review the status of each significant claim or legal proceeding and assess its potential financial exposure. If the potential loss from any claim, asserted or unasserted, or legal proceeding is considered probable and the amount can be reasonably estimated, we accrue a liability for the estimated loss. Because of uncertainties related to claims and litigation, accruals are based on our best estimates based on available information. On a periodic basis, as additional information becomes available, or based on specific events such as the outcome of litigation or settlement of claims, we may reassess the potential liability related to these matters and may revise these estimates, which could result in a material adverse adjustment to our operating results.

It is our policy to require our employees, consultants and parties to collaborative agreements to execute confidentiality agreements upon the commencement of employment or consulting relationships or collaborations with us. These agreements generally provide that all confidential information developed or made known during the course of the relationship with us is to be kept confidential and not to be disclosed to third parties except in specific circumstances. In the case of employees, the agreements also provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed by the individual during employment shall be our exclusive property to the extent permitted by applicable law.

License Agreements

In March 1996, we entered into a license agreement with the Medical Research Council (MRC) whereby MRC granted to us worldwide non-exclusive rights to certain patents related to the humanization and production of monoclonal antibodies. We pay MRC royalties on a quarterly basis with respect to sales of Soliris. The royalty is payable until the expiration of the last patent covered by the license agreement, which is expected to be in 2015, except that royalties for sales in Canada will continue until January of 2017. MRC may terminate the license if we file for bankruptcy or become insolvent, or if we fail to perform our obligations under the agreement and such failure is not remedied within three months after delivery of notice. Under the agreement, we agreed to (a) make royalty payments with respect to sales of licensed products, (b) promote the sale of Soliris of good marketable quality, and (c) use reasonable endeavors to meet market demand for licensed products.

We are party to other license agreements related to the manufacture and sale of Soliris. Under an existing arrangement with Lonza, Lonza produces commercial and clinical bulk quantities of Soliris. We pay Lonza royalties on a quarterly basis with respect to sales of Soliris manufactured at ARIMF. We have various agreements with Lonza, with commitments through 2018. Such commitments may be canceled only in limited circumstances. If we terminate certain supply agreements with Lonza without cause, we will be required to pay for product scheduled for manufacture under our arrangement.

In October 2012, we entered into a settlement and non-exclusive license agreement with a third party. Under the terms of the agreement, we made an upfront payment of approximately $38,000 in the fourth quarter of 2012 and will pay royalties on sales of Soliris in accordance with the terms of the agreement.

Government Regulation

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, are subject to extensive regulation by governmental authorities in the United States, the European Union and other territories. In the United States, 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. Soliris is regulated by the FDA as a biologic. Biologics require the submission of a Biologics License Application (BLA) and approval by the FDA prior to being marketed in the United States. Manufacturers of biologics 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 steps required before a biologic may be approved for marketing of an indication in the United States generally include:

(1) preclinical laboratory tests and animal tests;
(2) submission to the FDA of an IND 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;
(4) submission to the FDA of a BLA or supplemental BLA;
(5) FDA pre-approval inspection of product manufacturers; and
(6) FDA review and approval of the BLA or supplemental BLA.

Preclinical studies include laboratory evaluation, as well as animal studies to assess the potential safety and efficacy of the product candidate. Preclinical safety tests must be conducted in compliance with FDA regulations regarding good laboratory practices. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND 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.

Clinical trials involve the administration of the investigational product to healthy volunteers or to patients, under the supervision of qualified principal investigators. Each clinical study at each clinical site must be reviewed and approved by an independent institutional review board, prior to the recruitment of subjects.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap and different trials may be initiated with the same drug candidate within the same phase of development in similar or differing patient populations. Phase I studies may be conducted in a limited number of patients, but are usually conducted in healthy volunteer subjects. The drug is usually tested for safety and, as appropriate, for absorption, metabolism, distribution, excretion, pharmaco-dynamics and pharmaco-kinetics. Phase II usually involves studies in a larger, but still limited patient population to evaluate preliminarily the efficacy of the drug candidate for specific, targeted indications; to determine dosage tolerance and optimal dosage; and to identify possible short-term adverse effects and safety risks. Phase III trials are undertaken to further evaluate clinical efficacy of a specific endpoint and to test further for safety within an expanded patient population at geographically dispersed clinical study sites. Phase I, Phase II or Phase III testing might not be completed successfully within any specific time period, if at all, with respect to any of our product candidates. Results from one trial are not necessarily predictive of results from later trials. Furthermore, the FDA, sponsor or institutional review board may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The results of the preclinical studies and clinical trials, together with other detailed information, including information on the manufacture and composition of the product, are submitted to the FDA as part of a BLA requesting approval to market the product candidate for a proposed indication. Under the Prescription Drug User Fee Act, as amended, the fees payable to the FDA for reviewing a BLA, as well as annual fees for commercial manufacturing establishments

and for approved products, can be substantial. The BLA review fee alone can exceed $1,500, subject to certain limited deferrals, waivers and reductions that may be available. Each BLA submitted to the FDA for approval is typically reviewed for administrative completeness and

reviewability within 60 days following submission of the application. If found sufficiently complete, the FDA will “file” the BLA, thus triggering a full review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission. The FDA’s established goal is to review 90% of Priority BLA applications and original efficacy supplements within six months and 90% of Standard applications and original efficacy supplements in ten months, whereupon a review decision is to be made. The FDA, however, may not approve a drug within these established goals and its review goals are subject to change from time to time because the review process is often significantly extended by FDA requests for additional information or clarification. As part of its review, the FDA may refer the BLA to an advisory committee for evaluation and a recommendation as to whether the application should be approved. Although the FDA is not bound by the recommendation of an advisory committee, the agency usually has followed such recommendations.

Further, the outcome of the review, even if generally favorable, may not be an actual approval but instead a “complete response letter” communicating the FDA's decision not to approve the application, outlining the deficiencies in the BLA, and identifying what information and/or data (including additional pre-clinical or clinical data) is required before the application can be approved. Even if such additional information and data are submitted, the FDA may decide that the BLA still does not meet the standards for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than us.

Before approving a BLA, the FDA may inspect the facilities at which the product is manufactured and will not approve the product unless current Good Manufacturing Practices (cGMP) compliance is satisfactory. The FDA may deny approval of a BLA if applicable statutory or regulatory criteria are not satisfied, or may require additional testing or information, which can delay the appro