ALEXION PHARMACEUTICALS INC
Form 10-K
February 23, 2007
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(D) OF

THE SECURITIES AND EXCHANGE ACT OF 1934

x Annual report pursuant to Section 13 or 15 (d) of the Securities Exchange Act of 1934
For the fiscal year ended December 31, 2006

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 $.0001

Name of each exchange on which registered: The Nasdaq Stock Market LLC
Securities registered pursuant to Section 12(g) of the Act: None

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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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. Please see definition of accelerated and large accelerated filer in Rule 12b-2 of the Exchange Act. Check One:

Large Accelerated Filer: x Accelerated Filer: ¨ Non-Accelerated Filer: ¨

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 The Nasdaq Stock Market LLC on June 30, 2006, was approximately $1.063 Billion.

The number of shares of Common Stock outstanding as of February 21, 2007 was 35,740,970.

Portions of the registrant s Definitive Proxy Statement to be used in connection with its Annual Meeting of Stockholders to be held on May 3, 2007, are incorporated by reference into Part III of this report.

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PART I

On December 9, 2005, our Board of Directors unanimously approved a change to our fiscal year end from July 31 to December 31. In view of this change, this Form 10-K includes financial information (i) for the five month transition period from August 1, 2005 to December 31, 2005, which we refer to as the transition period throughout this report and (ii) for the years ended December 31, 2006, July 31, 2005, 2004 and 2003. We identify each fiscal year in this transition report according to the calendar year in which such fiscal year ends. For example, we refer to the fiscal year ended July 31, 2004, as fiscal 2004 or 2004.

Unless the context requires otherwise, references in this report to we, our, us, Company and Alexion refer to Alexion Pharmaceuticals, Inc. a 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 status of our ongoing clinical trials and prospects for regulatory approval, timing for completion of our ongoing clinical trials, evaluation of our clinical trial results by regulatory agencies, the need for additional research and testing, the uncertainties involved in the drug development process, the safety and efficacy of our product candidates, our future research and development activities, estimates of the potential markets for our products, assessment of competitors and potential competitors, estimates of the capacity of manufacturing and other facilities to support our products, the sufficiency of our existing capital resources and projected cash needs, sales and marketing plans, assessment of impact of recent accounting pronouncements as well as assumptions relating to the foregoing. Words such as anticipates, expects, intends, plans, believes, seeks, est 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 other reports or documents we file from time to time with the Securities and Exchange Commission.

Item 1. ***BUSINESS.***

Overview

We are a biotechnology company working to develop and deliver life-changing drug therapies for patients with serious and life-threatening medical conditions. We are engaged in the discovery and development of therapeutic products aimed at treating patients with a wide array of severe disease states, including hematologic diseases, cancer, and autoimmune disorders. Since our incorporation in January 1992, we have devoted substantially all of our resources to drug discovery, research, and product and clinical development. Since September 2005, we have formed a number of wholly-owned subsidiaries to support commercial and regulatory

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operations. In July 2006, we acquired a manufacturing plant in Smithfield, Rhode Island for the future commercial production of our products.

In September 2006, we filed a Biologics License Application, or BLA, with the U.S. Food and Drug Administration, or FDA, and a European Marketing Authorization Application, or MAA, in Europe, for Soliris (eculizumab) for the treatment of a rare, life-threatening blood disorder known as Paroxysmal Nocturnal Hemoglobinuria, or PNH. The Phase III clinical development program for Soliris (eculizumab) in PNH is comprised of two Phase III clinical trials, known as TRIUMPH and SHEPHERD. The FDA agreed to the design of the protocols for these two trials under the Special Protocol Assessment, or SPA, process. TRIUMPH is a placebo-controlled pivotal efficacy trial and SHEPHERD is an open-label, non-placebo controlled safety trial with efficacy secondary endpoints. In January 2006, we reported positive results from TRIUMPH, and the results were later published in the September 2006 issue of the New England Journal of Medicine. All pre-specified, primary and secondary endpoints in the TRIUMPH trial were achieved with statistical significance. In December 2006, we reported positive results from SHEPHERD. Soliris (eculizumab) appeared to be safe and well tolerated during the twelve month SHEPHERD trial, and all pre-specified primary and secondary efficacy endpoints in the SHEPHERD trial were achieved with statistical significance. Data from TRIUMPH and SHEPHERD served as the primary basis for the BLA and MAA submitted in the United States and Europe, respectively.

In November 2006, we received priority review designation for the Soliris (eculizumab) BLA from the FDA. Priority review status is granted by the FDA to products that, if approved, would be a significant improvement over existing therapies. Similarly, in August 2006, we announced that our Soliris (eculizumab) MAA was granted accelerated assessment by the European Medicines Agency, or EMEA, in Europe. Review under the Accelerated Assessment Procedure is provided by the EMEA for medicinal products of major therapeutic interest and shortens the timeframe for review by that agency. The granting of priority review for our BLA and accelerated assessment for our MAA does not ensure or increase the likelihood that our applications for regulatory approval of Soliris (eculizumab) will be approved. In November 2006, we also announced that the EMEA had validated the Soliris MAA allowing for commencement of the review process.

In addition to our Phase III PNH clinical program, we are conducting the following activities: (1) the EMBRACE Expanded Access Trial, (2) the EXPLORE diagnostics trial and (3) a global Patient Registry for PNH patients. The EMBRACE trial (The Paroxysmal Nocturnal Hemoglobinuria Early Access Treatment Protocol) was initiated in December 2006 to provide the investigational agent eculizumab in the United States to PNH patients in accordance with a Treatment Protocol authorized by the FDA. Treatment Protocols are designed to make promising investigational agents available for patients with serious or life-threatening diseases for which there are no comparable or satisfactory alternative therapies, before general marketing is authorized. We initiated the EXPLORE trial in August 2006 to investigate the frequency and clinical characteristics of undiagnosed PNH patients who have been diagnosed with other bone marrow failure diseases such as aplastic anemia and myelodysplasia. The global PNH Patient Registry involves the study of the natural history of PNH.

In addition to PNH, we are considering the evaluation of other potential indications for Soliris (eculizumab) as well as other formulations of eculizumab for additional clinical indications, and we are actively pursuing development of other antibody product candidates in early stages of development. During 2006, we completed a final Phase III trial of another product candidate known as pexelizumab with our partner for this product, Procter & Gamble Pharmaceuticals. After reviewing results from that trial, we along with Procter & Gamble Pharmaceuticals, have determined not to pursue further development of pexelizumab.

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To date, we have not received any revenues from the sale of our products. We have incurred operating losses since our inception. As of December 31, 2006, we had an accumulated deficit of approximately $638 million. We expect to incur substantial operating losses for the next several years due to expenses associated with product research and development, pre-clinical studies and clinical testing, regulatory activities, manufacturing development, scale-up and commercial-scale manufacturing, pre-commercialization activities, developing a sales and marketing force, and other infrastructure support costs. We may need to obtain additional financing to cover these costs.

In November 2006, we sold 3.45 million shares of our common stock in a registered offering at a price to the public of $43 per share resulting in proceeds of approximately $140 million, net of underwriting discount, fees and other expenses. We intend to use the net proceeds from this offering for general corporate purposes.

The Immune System

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
- disease-causing combinations of antigens and antibodies known as immune complexes.

When activated by 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 be activated inappropriately to direct an inflammatory response at healthy tissue, which may result in acute and chronic inflammatory conditions.

Hematologic, autoimmune, or inflammatory diseases in which the complement cascade is activated include:

- PNH;
- transplantation;
- Myasthenia Gravis;
- autoimmune hemolytic anemias;
- Guillain-Barre syndrome;
- rheumatoid arthritis;

autoimmune kidney disease;

lupus;

inflammatory skin and muscle disorders;

multiple sclerosis;

antiphospholipid syndrome; and

asthma

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Product Development Programs

We have focused our product development programs on anti-inflammatory therapeutics for diseases for which we believe current treatments are either non-existent or inadequate. Our lead product candidate, eculizumab, is a genetically altered antibody known as a C5 complement inhibitor, or a C5 Inhibitor, which is designed to selectively block the production of inflammation-causing proteins in the complement cascade. We believe that selective suppression of this immune response may provide a significant therapeutic advantage relative to existing therapies. Although we believe C5 Inhibitors may be useful in the treatment of a variety of diseases and conditions resulting from aberrant complement response, we are currently focusing our efforts on the development of our lead product candidate, Soliris (eculizumab), for the treatment of PNH.

Our pipeline programs are as follows:

Product Candidate	Indication	Clinical Trial	Status (a)
Soliris (eculizumab)	Paroxysmal Nocturnal Hemoglobinuria (PNH)	TRIUMPH (Phase III)	Statistically significant positive results announced January 2006
		SHEPHERD (Phase III)	Statistically significant positive results announced December, 2006
		Phase III Extension study	Enrollment ongoing
	Renal Transplantation		Pre-clinical research
	Autoimmune diseases		Pre-clinical research
Eculizumab (nebulized)	Asthma		Pre-clinical research
Eculizumab (Intravitreal)	Age-Related Macular Degeneration		Pre-clinical research
CD200 Mab	CLL, Multiple Myeloma		Pre-clinical research
DC-SIGN Mab	Cancer Vaccine		Pre-clinical research

C5 Inhibitors

Complement proteins are a series of inactive proteins circulating in the blood. When activated by stimuli, including those associated with both acute and chronic inflammatory disorders, these inactive complement proteins are split by enzymes known as convertases into activated byproducts through the complement cascade.

Some of these byproducts, notably C3b, are helpful in fighting infections and inhibiting autoimmune disorders. However, the byproducts generated by the cleavage of C5, known as C5a and C5b-9, generally cause harmful inflammation if inappropriately or over-activated. The inflammatory byproducts of C5 cause:

- lysis, or destruction, of red blood cells that are deficient in complement inhibitors;
- activation and destruction of muscle and other tissue cells;

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activation of white blood cells;

attraction of white blood cells;

production of inflammatory chemicals including tumor necrosis factor-alpha;

activation of blood vessel-lining cells called endothelial cells, allowing leakage of white blood cells into tissue;

activation of kidney cells; and

initiation of cell suicide programs in heart cells

The following diagram illustrates the complement cascade:

Because of the generally beneficial effects of the components of the complement cascade prior to C5 and the greater inflammatory, destructive and disease-promoting effects of the cleavage products of C5, we have identified C5 as a potentially effective anti-inflammatory drug target. Our C5 Inhibitor, eculizumab, specifically and tightly binds to C5 blocking its cleavage into harmful byproducts, which we believe may inhibit subsequent damage from the inflammatory response.

In laboratory and animal models of human disease, we have shown that the administration of a C5 Inhibitor, as compared to placebo, has demonstrated the following:

prevention of lysis of red blood cells;

prevention of inflammation during cardiopulmonary bypass;

reduction of heart tissue damage during myocardial infarction;

reduction of brain damage in cerebral ischemia, or reduced blood flow to brain tissue;

enhancement of survival in a model of lupus;

preservation of kidney function in nephritis, or inflammation of kidney tissue;

prevention and amelioration of asthmatic attacks; and

enhancement of survival in organ transplantation models.

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In addition, in human clinical trials, we have shown that C5 Inhibitors may be associated with:

- reduction of red blood cell destruction, improvement in anemia, amelioration of fatigue and reduction of blood clots in PNH patients;
- reduction of an objective measure of disease activity in rheumatoid arthritis patients; and
- reduction of the incidence of proteinuria in lupus patients.

C5 Inhibitor Immunotherapeutic Product Candidates

We are developing our lead C5 Inhibitor product candidate, Soliris (eculizumab), for the treatment of inflammation related to chronic hematologic disorders and autoimmune disorders. The initial indication for which we are pursuing development of Soliris (eculizumab) is PNH.

To date, eculizumab has been observed to be reasonably well tolerated in completed clinical trials in which over 900 individuals were treated with eculizumab; 195 of these individuals were PNH patients enrolled in trials studying PNH. Our other C5 Inhibitor, pexelizumab, has been observed to be reasonably well tolerated in completed clinical trials in which over 10,000 individuals were treated with either pexelizumab or placebo.

Lead Eculizumab Indication

Eculizumab is a humanized antibody that blocks complement activity for one to two weeks after a single dose at the doses currently tested, and is designed for the chronic treatment of hematologic disorders such as PNH and autoimmune diseases. Results of the two Phase III clinical trials for Soliris (eculizumab) in PNH showed statistically significant achievement of all primary and secondary endpoints. We have filed for authorization to market Soliris (eculizumab) for PNH patients with the FDA and the EMEA in the United States and Europe, respectively. We have retained full commercial rights to Soliris (eculizumab) worldwide.

About Paroxysmal Nocturnal Hemoglobinuria or PNH

We are developing eculizumab for treatment of patients afflicted with the chronic hematologic disorder, Paroxysmal Nocturnal Hemoglobinuria, or PNH. PNH is a life-threatening, rare acquired genetic deficiency blood disorder characterized by severe anemia and risk of blood clotting, or thrombosis. 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 may suffer from chronic 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 frequent bouts of hemoglobinuria or release of blood cell hemoglobin into the urine, abdominal pain, painful swallowing, high blood pressure in the lungs, disabling fatigue, and a poor quality of life. The red blood cell destruction may be sufficiently large that recurrent blood transfusions are necessary to support normal red blood cell function. The hemolysis in patients with PNH may be associated with severe, life-threatening blood clots. The prevalence, or number of affected patients at any one time, has not been definitively determined but can be estimated at approximately 8,000 10,000 total patients in North America and Western Europe. Approximately one-half of the patients with PNH die from the disease within 10-15 years of diagnosis. Currently there is no U.S. Food and Drug Administration approved therapy for PNH. In 2003, the FDA and the European Medicines Agency, or EMEA, each granted Orphan Drug Status for the development of eculizumab in PNH.

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Clinical Trials PNH

In September 2006, we submitted a Biologics License Application, or BLA, with the U.S. Food and Drug Administration, or FDA, and a European Marketing Authorization Application, or MAA, in Europe, for Soliris (eculizumab) for the treatment of PNH. Data from two clinical trials that comprised the pivotal Phase III program, known as the TRIUMPH and SHEPHERD trials, served as the primary basis for the BLA and MAA. In July 2004, we received written confirmation from the FDA indicating agreement with the protocol designs for the TRIUMPH and SHEPHERD trials. The agreement for the Phase III program was reached under the FDA s Special Protocol Assessment, or SPA, process, a procedure by which the FDA provides official evaluation and guidance on proposed protocols for pivotal Phase III clinical trials. Similarly, we have obtained protocol assistance from the EMEA with respect to the pivotal Phase III PNH program in Europe. Prior to submission of the BLA and MAA for Soliris (eculizumab) in PNH, we also presented and discussed available Phase III results with the FDA and EMEA. In 2003, the FDA and the EMEA granted Orphan Drug designation for the development of Soliris (eculizumab) in PNH. We retain all rights to eculizumab in all indications worldwide.

On January 26, 2006, we reported positive results with Soliris (eculizumab) in the pivotal Phase III TRIUMPH trial in PNH patients and published the trial results in the September 20, 2006 issue of the New England Journal of Medicine. TRIUMPH is a double-blind, randomized, placebo-controlled multi-center pivotal Phase III trial, examining the effects of eculizumab on the co-primary endpoints of hemoglobin stabilization and blood transfusion requirement in hemolytic, transfusion-dependent PNH patients during six months of therapy. The pre-specified co-primary endpoints in the TRIUMPH trial (median transfusion rate and hemoglobin stabilization) were each achieved with statistical significance. The median transfusion rate was reduced from 10 units/patient with placebo to 0 units/patient with eculizumab ($p<0.000000001$). Hemoglobin stabilization was achieved by 49% of eculizumab patients as compared to 0% for placebo ($p<0.0000001$). Soliris (eculizumab) reduced intravascular hemolysis, as shown by the 85.8% lower median area under the curve for lactate dehydrogenase in the eculizumab group, as compared with the placebo group (58,587 vs. 411,822 U per liter × day; $P<0.001$). Clinically and statistically significant improvements in fatigue were observed as measured by scores on the Functional Assessment of Chronic Illness Therapy-Fatigue instrument ($P<0.001$) and the fatigue subscale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) ($P<0.001$). Treatment with Soliris (eculizumab) also significantly improved overall health and patient functioning as measured by the EORTC QLQ-C30 instrument including global health status ($P<0.001$) and all five aspects of patient functioning: role ($P<0.001$), social ($P=0.003$), cognitive ($P=0.002$), physical ($P<0.001$) and emotional ($P=0.008$). Treatment also significantly reduced EORTC QLQ-C30 disease-related symptoms including pain ($P=0.002$), dyspnea ($P<0.001$), appetite loss ($P<0.001$), and insomnia ($P=0.014$). Additionally, Soliris (eculizumab) appeared to be well tolerated with an adverse event profile comparable to placebo. The most frequent adverse events with Soliris (eculizumab) were headache, nasopharyngitis (or cold symptoms) and back pain. The study enrolled patients in the U.S., Canada, Europe, and Australia.

In December 2006, we reported positive results with Soliris (eculizumab) in the Phase III SHEPHERD trial in PNH Patients. SHEPHERD trial was an open-label, twelve-month non-placebo controlled trial primarily aimed at generating additional safety data with eculizumab in 97 PNH patients in the United States, Canada, Europe, and Australia, and included a primary surrogate of efficacy and additional efficacy endpoints. Results from the SHEPHERD trial showed that Soliris (eculizumab) appeared to be safe and well tolerated and provided clinically and statistically significant improvements in intravascular hemolysis, anemia, fatigue and quality of life. Results from the SHEPHERD trial were presented in December 2006 at the 48th Annual Proceedings of the American Society of Hematology. Soliris (eculizumab) therapy in SHEPHERD improved

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the intravascular hemolysis, as shown by a reduction in the median LDH area under the curve (-632,264 U/L W day; P<0.001). LDH levels during the study were reduced 87% from a median of 2051 U/L at baseline to 269 U/L after 12 months of treatment (P<0.001). Clinically and statistically significant improvements in fatigue were observed as measured by change from baseline using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) instrument (P<0.001) and the fatigue scale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) instrument, a standard questionnaire developed to assess quality of life in cancer patients particularly suffering from severe fatigue and anemia (P<0.001). Treatment with Soliris (eculizumab) also significantly improved overall health and patient functioning as measured by the EORTC QLQ-C30 instrument including the global health status scale (P<0.001) and all five aspects of patient functioning: role (P<0.001), social (P<0.001), cognitive (P<0.001), physical (P<0.001) and emotional (P<0.001). Treatment also significantly improved 7 of 9 EORTC QLQ-C30 symptom scales and single item measures including pain (P<0.001), dyspnea (P<0.001), appetite loss (P<0.001), and insomnia (P<0.001). Clinically and statistically significant improvements in anemia were also observed with eculizumab therapy as evidenced by the reduction in transfusion requirements from a median of 8.0 packed red cells in the 12 month pre-treatment period to 0.0 units during the 12 months of treatment (P<0.001). Additionally, 51% of patients in SHEPHERD were transfusion independent for the entire 12 month treatment period (P<0.001). Other improvements in anemia included a 44% increase in the endogenous PNH red blood cell mass (P<0.001) and an increase in hemoglobin levels from 9.2g/dl at baseline to 10.2g/dl after 12 months of treatment (P<0.001).

Prior to SHEPHERD and TRIUMPH, we conducted a three-month, open-label study in 11 PNH patients, results of which were reported in the February 5, 2004 issue of the New England Journal of Medicine. Patients treated with Soliris (eculizumab) experienced a substantial decrease in the destruction of PNH red blood cells, with the mean percentage of these cells increasing from 36.7 percent of the total population found in the body to 59.2 percent (P=0.005), and lactate dehydrogenase levels, a biochemical marker of red blood cell destruction, falling from a mean of 3,111 IU per liter to a mean of 594 IU per liter (P=0.002). This reduction in PNH red blood cell destruction helped reduce the median patient transfusion rates from 1.8 units per patient, per month, to 0.0 units per patient, per month (P=0.003). Episodes of hemoglobinuria were reduced by an average of 96 percent (P<0.001) and quality of life measurements, using EORTC QLQ C-30, substantially improved during treatment. Soliris (eculizumab) appeared reasonably well tolerated in this trial. Adverse events reported for Soliris (eculizumab) or placebo were similar in type and frequency to those reported in other controlled trials of eculizumab. The most common adverse events were headache, upper respiratory infection, muscle/joint aches, and influenza-like symptoms, and the severe adverse events were viral chest infection, dizziness and shivering. In the June 2005 issue of the journal *Blood*, we reported on the safety and sustained effects of Soliris (eculizumab) in a 52-week extension of our pilot open-label PNH trial in 11 patients. In this study, patients who received Soliris (eculizumab) continued to tolerate the drug reasonably well and experienced reduced hemolysis resulting in an increase in PNH red blood cells, a reduction in the need for transfusion, and improvements in multiple quality of life measures. Reported adverse events occurring in three or more patients were flu-like symptoms, sore throat, pain, nausea, bruising, cough, and upper respiratory infection. The adverse event profile for eculizumab-treated patients in this study was similar to that of placebo-treated patients in other patient population trials of eculizumab.

Patients who have completed the TRIUMPH and SHEPHERD trials, as well as patients that have completed the initial, open-label clinical trial, have been enrolled in an open-label extension trial to further evaluate safety data in PNH patients treated with Soliris (eculizumab).

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Eculizumab in Pre-Clinical Research Programs

Renal Transplantation

Solid-organ transplantation is an effective form of therapy for the management of patients with end-stage kidney, heart, lung, or liver failure. The rejection of the donor organ is usually managed by treatment of the recipient with immunosuppressive drugs that block the action of white blood cells to reject the donor organ. However, some potential transplant recipients have highly sensitized immune systems due to previous transplants, transfusions or pregnancies, or incompatibility with the blood type of the donor. In these presensitized graft recipients, antibody-mediated rejection, or AMR, is a major impediment to successful transplantation.

In collaboration with investigators at the Multi-Organ Transplant Program, London Health Sciences Centre, London, Ontario, Canada, we reported in the May 2005 issue of the journal *Transplantation* that inhibition of terminal complement using an anti-C5 complement-blocking antibody successfully prevented AMR in a rodent model of transplantation. Furthermore, addition of anti-C5 antibody to standard anti-cellular therapy resulted in a marked and significant increase in graft survival as compared to graft survival in animals treated with anti-cellular therapy alone. Importantly, AMR was prevented by anti-C5 antibody even in the presence of high levels of circulating anti-donor antibodies.

These data are supported by other studies that demonstrate an important role for terminal complement in antibody-mediated transplant rejection and suggest that complement blockade at C5 may be an effective therapy in patients who are either presensitized or who have received a blood type mismatched transplant organ. We are currently in pre-clinical studies to evaluate solid-transplantation as an indication for eculizumab.

Asthma

Asthma is a chronic respiratory disease that results in bronchial inflammation and airway constriction that prompts asthma s hallmark symptoms shortness of breath, chest tightness and wheezing.

In May 2005, we announced the results of a new animal model study that showed that treatment with an anti-C5 complement blocking antibody significantly reduced bronchial inflammation and airway constriction. The study, conducted by our researchers, the Yale University School of Medicine, and the Brigham and Women s Hospital, was published in the June 2005 issue of the Journal of Clinical Investigation.

The study suggested that both C5a and C5b-9 contribute to the initiation of airway inflammation and in immediate and sustained airway hyperreactivity. Importantly, the researchers found that animals given an anti-C5 blocking antibody either systemically or when inhaled through a nebulizer (a common asthma inhalation device) showed substantial reductions in airway reactivity even in the face of airway challenges with methacholine, a drug administered to confirm an asthma diagnosis.

The anti-C5 blocking antibody, unlike existing asthma therapies high-dose inhaled and oral corticosteroids blocked a wide range of inflammatory mediators known to contribute to the severity and persistence of asthma, including white blood cells and inflammatory mediators from eosinophils and neutrophils. These data suggest a direct role for complement-mediated inflammation in the pathogenesis of severe asthma. We are currently in pre-clinical studies to evaluate asthma as an indication for eculizumab.

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Antibody Discovery Technology Platform

Combinatorial Human Antibody Library Technologies

In order to expand our pipeline of potential antibody therapeutics, in September 2000, we acquired Prolifaron, Inc., a privately held biopharmaceutical company and integrated this entity into Alexion as a wholly-owned subsidiary, Alexion Antibody Technologies, Inc. or AAT. The AAT technology includes extensive research expertise and methodologies that we call Combinatorial Human Antibody Library Technologies or CoALT, in the area of creating fully human antibodies from libraries containing billions of human antibody genes. During 2006, we decided to relocate CoALT and other AAT technologies to our expanded research and discovery groups in our Cheshire, Connecticut headquarters. As a result, we initiated an integration plan with AAT to consolidate certain functions and operations, including the termination of all AAT personnel and possible disposal of equipment in that facility.

Our goal, through CoALT and related technologies, is to develop new fully human therapeutic antibodies addressing multiple disease areas, including autoimmune and inflammatory disorders, cancer and infectious disease. These technologies involve, in part, the generation of diverse libraries of human antibodies derived from patients blood samples, and the screening of these libraries against a wide array of potential drug targets. We believe that these technologies may be optimally suited to the rapid generation of novel, fully human and humanized, therapeutic antibodies directed at validated clinical targets. To date, we have focused on identifying antibodies that may be therapeutically effective in different cancers, autoimmune or inflammatory disorders, and infectious diseases. In addition, we believe that these technologies could permit the pre-clinical validation of new gene targets that are being identified by numerous groups from recent access to the human genome. We also believe that these technologies might identify therapeutic antibodies when the libraries are screened against certain of these new gene targets.

Pre-Clinical Programs

Anti-CD200 Antibody

We are developing an antibody for the treatment of B-Chronic Lymphocytic Leukemia (B-CLL), an incurable chronic cancer that results from expansion of B-lymphocytes and other myeloid tumors such as mulitple myeloma (MM). Our antibody binds to CD200, a molecule that is upregulated on the surface of B-CLL and MM tumor cells. CD200 normally acts as a potent immunosuppressant by interacting with the CD200 Receptor on macrophages and thereby sending an inhibitory signal to the macrophage. We believe upregulation of CD200 on the CLL and MM cell surface allows the tumor to inhibit the body s immune response to the tumor. Our antibody targets CLL and MM cells and blocks the interaction of CD200 with the CD200 Receptor with the objective of enhancing the body s immune response to these tumors. We have recently demonstrated the potent anti-tumor activity of our anti-CD200 antibody in a model of CLL, which was published in the January 2006 issue of the Proceedings of the National Academy of Sciences and presented at the 2006 meeting of the American Society for Clinical Oncology. Our anti-CD200 antibody drug candidates may have therapeutic application in patients suffering from B-CLL, MM and other blood and solid tumors with elevated CD200 expression.

Dendritic Cell Antibodies

We are developing humanized antibodies to newly discovered cell surface proteins, DC-SIGN, found exclusively on human dendritic cells, a type of human immune cell, and a related receptor, L-SIGN. Under the

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exclusive worldwide license agreement and research alliance with the University Medical Center of Nijmegen, The Netherlands, we received rights related to these molecules and any associated therapeutic product candidates, including already identified monoclonal antibodies. These products may have broad therapeutic application in several clinical settings including different cancers and infectious diseases, and in certain inflammatory disorders. This alliance broadens our interest in immune system modulation to also include human dendritic cells.

Dendritic cells have recently come to be appreciated as critical controllers of the immune system. In order for an immune response against foreign antigens to occur, these antigens must be displayed by so-called antigen-presenting cells. While dendritic cells are an extremely rare immune cell type, they are the most potent of all the antigen presenting cells. Dendritic cells capture antigens in the peripheral tissues, process and display the antigen fragments on their cell surface, and then migrate from the periphery to the T-cell areas of the lymphoid organs. There they attract resting T-cells and present their antigen load, thus activating the T-cells to begin an immune response. This process appears to be controlled in part by the newly identified molecule DC-SIGN. We have recently demonstrated that our DC-SIGN antibody potently activates the immune system and exhibits significant anti-tumor activity in a model system. These results were recently presented at the 2006 meeting of the American Society for Clinical Oncology

Anti-MBL Antibody

We are developing an antibody that blocks complement activation via the Lectin Pathway. This inflammatory pathway is initiated by the binding of a specific protein, known as MBL, to targets on the surface of activated endothelial cells and may represent a major cause of inflammation and heart damage. Under a license agreement with The Brigham and Women s Hospital, Inc., we received exclusive worldwide rights to novel anti-inflammatory technologies and to associated therapeutic products, including a potent monoclonal antibody against MBL. The anti-MBL approach may have broad therapeutic application in patients suffering from various vascular disorders as well as some chronic inflammatory conditions.

The CuraGen Corporation Agreement for Target Discovery

We completed a drug target discovery and validation program with CuraGen Corporation focused on oncology, the study of tumors and/or cancers. This agreement enabled us and CuraGen to leverage our respective areas of expertise to discover and validate novel biologic and small molecule targets for use in developing pharmaceutical products.

Under the agreement, CuraGen applied its integrated functional genomic technologies to identify potential drug targets derived from our supplied research materials, and will retain the rights to potential non-antibody protein therapeutics across all disease areas. We are using our CoALT antibody discovery platform to determine the therapeutic utility of the targets. We own preferential rights to develop and commercialize some antibody and small molecule therapeutics against drug targets across all disease areas. CuraGen is eligible to receive licensing fees, development milestone payments and sales royalties from pharmaceutical products stemming from this alliance. CuraGen retains the right to develop or out license some candidates from the program.

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Other Pre-Clinical Programs

Anti-TPO Receptor Antibody

In December 2003, we and XOMA entered into a collaborative agreement for the development and commercialization of a rationally designed human c-MPL agonist antibody to treat chemotherapy-induced thrombocytopenia. Thrombocytopenia is an abnormal blood condition in which the number of platelets is reduced, potentially leading to bleeding complications. In November 2004, we and XOMA determined that the lead molecule in this c-MPL agonist antibody collaboration did not meet the criteria established in the program for continued development. We and XOMA agreed not to continue with this joint development program and terminated the collaboration in April 2005. Under the terms of the agreement, we received a $1.5 million upfront non-refundable payment upon initiation of the collaboration. We recorded the payment as a deferred research and development payment. During the quarter ended April 30, 2005, we recognized the remaining balance of approximately $1.3 million of the deferred payment as a reduction of research and development expense.

Strategic Alliance with Procter & Gamble

In January 1999, we entered into collaboration with P&G with respect to the joint development of pexelizumab in cardiovascular indications. In December 2001, we and P&G entered into a binding memorandum of understanding, or MOU, pursuant to which we and P&G revised our January 1999 collaboration. During 2006, we announced that results from the final Phase III clinical trial of pexelizumab did not achieve its primary endpoint, and that this trial and prior Phase III trials of pexelizumab will not be sufficient for filing for licensing approval. We have held discussions with P&G regarding the pexelizumab program, and we do not expect to continue development of pexelizumab with P&G or in the indications studied with P&G.

Under the revised structure per the MOU, we and P&G share decision-making and responsibility for all U.S. development and commercialization costs for pexelizumab, including clinical, manufacturing, marketing, and sales efforts. Prior to December 2001, P&G was generally funding all clinical development and manufacturing costs for pexelizumab. The revised collaboration per the MOU provides that we and P&G each incur approximately 50% of all Phase III clinical trial, product development and manufacturing, and commercialization costs necessary for the potential approval and marketing of pexelizumab in the U.S. and that we would receive approximately 50% of the gross margin on U.S. sales, if any. Under the MOU, P&G agreed to retain responsibility for future development and commercialization costs outside the U.S. and we would receive royalties on sales outside the U.S., if any. We would be responsible for paying royalties and licensing fees on certain third party intellectual property worldwide, if such intellectual property were necessary in order to commercialize pexelizumab. Additionally, as part of the MOU, we would receive milestone payments for achieving specified development steps, regulatory filings and approvals, but not for previously agreed sales milestones and we would generally forego further research and development support payments from P&G.

Reimbursements received by us from P&G in connection with P&G s share of our services and related personnel are recorded as a reduction of research and development and market research expense. As part of the revised collaboration per the MOU, P&G funded 100% of the costs for the two acute myocardial infarction, or AMI, Phase II clinical trials. We and P&G agreed, as per the MOU, that we share concurrently 50% of the ongoing U.S. pre-production and development manufacturing costs for pexelizumab as well as any future AMI or CABG Phase III clinical trial costs.

P&G has the right to terminate the collaboration or sublicense its collaboration rights at any time. If P&G terminates the collaboration, P&G is required to contribute its share of agreed to obligations and costs incurred

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prior to termination, but may not be required to contribute towards costs incurred after termination. In the event that P&G were to terminate the collaboration, all rights and the exclusive license to our intellectual property related to pexelizumab would revert to us. The MOU does not contemplate any payments to P&G in the event P&G were to terminate the collaboration; however, P&G might seek to negotiate such a payment or might seek to sublicense its collaboration rights rather than terminate the collaboration.

Manufacturing

We obtain drug product to meet our requirements for clinical studies using both internal and third-party contract manufacturing capabilities. We currently rely on a third-party contract manufacturer for our anticipated eculizumab commercial needs, and intend to equip and qualify our own manufacturing facility for anticipated eculizumab commercial needs in the future. For both clinical requirements and anticipated commercial requirements, we have contracted and expect to continue contracting for product finishing, vial filling, and packaging through third parties.

In July 2006, we acquired a manufacturing plant in Smithfield, Rhode Island. We intend to equip and develop the plant in accordance with FDA and other regulatory requirements to manufacture Soliris (eculizumab) and other product candidates. We have a pilot manufacturing plant suitable for the production and purification of certain of our product candidates for clinical studies. The pilot manufacturing plant is currently being decommissioned and transferred to the Smithfield, Rhode Island plant.

Our most significant agreement with a third party manufacturer is the Large-Scale Product Supply Agreement, or the Lonza Agreement, dated December 18, 2002 with Lonza Biologics PLC, or Lonza, relating to the manufacture of our product candidate eculizumab. The Lonza Agreement was amended, or the Lonza Amendment, on April 9, 2004. Per the Lonza Agreement, we have remitted cash advances aggregating $13.5 million through December 31, 2006. If we terminate the Lonza Agreement we may be required to pay for batches of product scheduled for manufacture up to 12 months following termination.

The amounts paid to Lonza in consideration of the Lonza Agreement are accounted for as prepaid manufacturing costs within the accompanying balance sheet and are recognized as additional manufacturing costs as the batches are manufactured. On a quarterly basis, we evaluate our plans to proceed with production under the Lonza Agreement, considering our commercialization plans for Soliris (eculizumab). In addition, we evaluate the prepaid manufacturing costs against estimated net realizable value, or NRV. If estimated NRV is not positive, then all or a portion of the prepaid manufacturing cost may be recognized as an expense.

Sales and Marketing

We currently have established core marketing capabilities and have begun to establish sales and distribution capabilities. We are developing our own specialized sales force and marketing organization to market Soliris (eculizumab) in the United States and in Europe. We will need to continue developing or will have to contract with others to obtain these capabilities to commercialize Soliris (eculizumab) successfully. We may promote Soliris (eculizumab) in collaboration with marketing partners or rely on relationships with one or more companies with established distribution systems and direct sales forces, either in the United States or in other countries.

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Patents and Proprietary Rights

Patents and other proprietary rights are important to our business. Our policy 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 to develop and maintain our competitive position, as well as patents that we have licensed or may license from other parties.

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 January 31, 2007, we own or in-license over 77 U.S. patents and 61 U.S. patent applications. These patents and patent applications relate to technologies or products in the C5 Inhibitor program, high throughput screening, vectors, cancer, the MBL program, recombinant antibodies, the dendritic cell program, and other technologies. We own or in-license 58 foreign patents and 167 pending foreign patent applications. We will owe royalties and other fees to the licensors of some of those patents and patent applications in connection with any future commercial manufacture and sale of our product candidates, including eculizumab.

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.

We are aware of broad patents owned by third parties relating to the manufacture, use, and sale of recombinant humanized antibodies, recombinant humanized single-chain antibodies, recombinant human antibodies and recombinant human single-chain antibodies. Many of our product candidates are genetically engineered antibodies, including recombinant humanized antibodies, recombinant humanized single chain antibodies, recombinant human antibodies, or recombinant human single chain antibodies. We have received notices from the owners of some of these patents in which the owners claim that some of these patents may be infringed by the development and commercialization of some of our drug candidates, including eculizumab. We are also aware of other patents owned by third parties that might be claimed to be infringed by the development and commercialization of some of our drug candidates, including eculizumab. We have acquired licenses to certain of these patents which we believe are relevant for the expeditious development and commercialization of eculizumab and certain of our other products as currently contemplated. With regard to certain other patents, we have either determined in our judgment that the patents are invalid, that our products do not infringe the patents, or that we can license such patents on commercially reasonable terms, or we have identified and are testing

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various approaches which we believe should not infringe the patents and which should permit commercialization of our products. If our judgment is incorrect, and we are unable to acquire a license to a necessary patent on commercially reasonable terms, our ability to commercialize our products, including eculizumab, could be significantly adversely affected or could be prevented.

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 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.

Government Regulation

The pre-clinical studies and clinical testing, manufacture, labeling, storage, record keeping, advertising, promotion, export, and marketing, among other things, of our proposed products, including Soliris (eculizumab), are subject to extensive regulation by governmental authorities in the U.S. and other countries. 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. We believe that Soliris (eculizumab) will be regulated by the FDA as a biologic. Biologics require the submission of a Biologics License Application, or BLA, and approval by 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 pending 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 in the U.S. generally include:

(1) pre-clinical laboratory tests and animal tests;

(2) submission to the FDA of an Investigational New Drug 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;

(4) submission to the FDA of a BLA;

(5) FDA pre-approval inspection of product manufacturers; and

(6) FDA review and approval of BLA.

The testing and approval process requires substantial time, effort and financial resources, and we cannot assure you that any approval will be granted on a timely basis or at all, for Soliris (eculizumab) or any other product.

Pre-clinical studies include laboratory evaluation, as well as animal studies to assess the potential safety and efficacy of the product candidate. Pre-clinical safety tests must be conducted in compliance with FDA

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regulations regarding good laboratory practices. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an Investigational New Drug Application, or 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 are closely monitored and 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 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.

Under the Special Protocol Assessment procedure, a sponsor may seek the FDA s agreement on the design and size of a clinical trial intended to form the primary basis of an effectiveness claim. If the FDA agrees in writing, its agreement may not be changed after the trial begins, except in limited circumstances. If the outcome of the trial is successful, the sponsor will ordinarily be able to rely on it as the primary basis for approval with respect to effectiveness. The Phase III clinical program for Soliris (eculizumab) for the PNH indication was conducted pursuant to an SPA. There can be no assurance that the FDA will agree to the design and size of future clinical trials, and there can be no assurance that any trial will have a successful outcome.

The results of the pre-clinical 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. Under the Prescription Drug User Fee Act, as amended, the fees payable to 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 $500,000, subject to certain limited deferrals, waivers and reductions that may be available. Each BLA submitted to FDA for approval is typically reviewed for administrative completeness and reviewability within 45 to 60 days following submission

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of the application. If found complete, the FDA will file the BLA, thus triggering substantive review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable. In November 2006, we announced that the FDA has accepted our BLA for filing, thereby triggering the substantive review. The FDA s established goals for the review of BLAs is six months for priority applications and 10 months for regular applications. Also in November 2006, we announced that FDA has granted Priority Review for the Soliris (eculizumab) BLA. The FDA is not legally obligated, however, to complete its review within these established goals and its review goals are subject to change from time to time. Further, the outcome of the review, even if generally favorable, typically is not an actual approval but an action letter that describes additional work that must be done before the application can be approved. 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, or 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 approval process. FDA approval of any application may include many delays or never be granted. If a product is approved, the approval will impose limitations on the indicated uses for which the product may be marketed, require that warning statements be included in the product labeling, require that additional studies be conducted following approval as a condition of the approval, impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. To market for other indicated uses, or to make certain manufacturing or other changes requires FDA review and approval. Further post-marketing testing and surveillance to monitor the safety or efficacy of a product may be required. Also, product approvals may be withdrawn if compliance with regulatory standards is not maintained or if safety or manufacturing problems occur following initial marketing. Finally, new government requirements may be established that could delay or prevent regulatory approval of Soliris (eculizumab) and our other products under development.

The U.S. Congress and regulatory authorities, including the FDA, are considering whether an abbreviated approval process for so-called generic or follow-on biological products should be adopted. An abbreviated approval process is currently available for generic versions of conventional chemical drug compounds, sometimes referred to as small molecule compounds, but not for biological products approved under the Public Health Service Act through a BLA. Currently, an applicant for a generic version of a small molecule compound only has to reference in its application an approved product for which full clinical data demonstrating safety and effectiveness exist for the approved conditions of use; demonstrate that its product has the same active ingredients, dosage form, strength, route of administration and conditions of use and is absorbed in the body at the same rate and to the same extent as the referenced approved drug; include certifications to patents listed with the FDA for the referenced approved drug; and await the expiration of any non-patent exclusivity. Various proposals have been made to establish an abbreviated approval process to permit approval of generic or follow-on versions of biological products. It is unclear as to when, or if, any such proposals may be adopted but any such abbreviated approval process could have a material impact on our business as follow-on products would be significantly less costly to bring to market and may be priced significantly lower than our products would be.

Both before and after the FDA approves a product, the manufacturer and the holder or holders of the BLA for the product are subject to comprehensive regulatory oversight. For example, quality control and manufacturing procedures must conform to cGMP requirements after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to spend time, monies, and effort to maintain cGMP compliance.

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Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which generally is a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are publicly disclosed by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. If a product which has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, i.e., the FDA may not approve any other applications to market the same drug for the same indication for a period of seven years, except in limited circumstances. Soliris (eculizumab) was granted Orphan Drug designation for the PNH indication by the FDA in 2003.

Foreign Regulation

In addition to regulations in the United States, we are subject to a variety of foreign regulatory requirements governing human clinical trials and marketing approval for drugs. The foreign regulatory approval process includes all of the risks associated with FDA approval set forth above as well as additional country-specific regulations. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

For example, under European Union regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

During November 2006, we announced that the European Medicines Agency, or EMEA, has validated our submission of a Marketing Authorization Application, or MAA, for Soliris (eculizumab) that we had submitted in September 2006. This step commences the review process of the MAA. In addition, the EMEA has notified us that they will utilize their Accelerated Assessment Procedure for review of the Soliris (eculizumab) MAA. Accelerated Assessment is given for medicinal products of major therapeutic interest and shortens the timeframe for review by the EMEA.

Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of coverage and the amount of reimbursement from government programs, including Medicare and Medicaid in the United States, and other third-party payers . These health insurance programs may restrict coverage of some products. Many third-party payers use formularies, under which only selected drugs are covered, variable co-payments that make drugs that are not preferred by the payor more expensive for patients, and utilization management controls, such as requirements for prior authorization or failure on another type of treatment, before the payer will cover a

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particular drug. Payers may especially impose these obstacles to coverage for higher-priced drugs, as Soliris (eculizumab) is likely to be.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market.

Since Soliris (eculizumab) will likely be too expensive for most patients to afford without health insurance coverage, adequate coverage and reimbursement by third-party payers is essential to our ability to successfully commercialize Soliris (eculizumab).

Competition

Currently, many companies, including major pharmaceutical and chemical companies as well as specialized biotechnology companies, are engaged in activities similar to our activities. Universities, governmental agencies and other public and private research organizations also conduct research and may market commercial products on their own or through joint ventures. These companies and organizations are in the U.S., Europe and elsewhere. Many of these entities may have:

- substantially greater financial and other resources;
- larger research and development staffs;
- lower labor costs; and/or
- more extensive marketing and manufacturing organizations.

Many of these companies and organizations have significant experience in pre-clinical testing, human clinical trials, product manufacturing, marketing, sales and distribution and other regulatory approval and commercial procedures. They may also have a greater number of significant patents and greater legal resources to seek remedies for cases of alleged infringement of their patents by us to block, delay, or compromise our own drug development process.

We compete with large pharmaceutical companies that produce and market synthetic compounds and with specialized biotechnology firms in the U.S., Europe and elsewhere, as well as a growing number of large pharmaceutical companies that are applying biotechnology to their operations. Many biotechnology companies have focused their developmental efforts in the human therapeutics area, and many major pharmaceutical companies have developed or acquired internal biotechnology capabilities or have made commercial arrangements with other biotechnology companies. A number of biotechnology and pharmaceutical companies are developing new products for the treatment of the same diseases being targeted by us; in some instances, these products have already entered clinical trials or are already being marketed. Other companies are engaged in research and development based on complement proteins.

Each of Adprotech Ltd., Avant Immunotherapeutics, Inc., Baxter International Inc., Tanox, Inc., XOMA Ltd., Novo Nordisk A/S, and Archemix Corporation has publicly announced intentions to develop complement

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inhibitors to treat diseases related to trauma, inflammation or certain brain or nervous system disorders. We are also aware that Abbott Laboratories Inc., Baxter International, Inc., Millenium Pharmaceuticals, Inc. and Neurogen Corporation have had programs to develop complement inhibitor therapies. We believe that our potential C5 Inhibitors differ substantially from those of our competitors due to our compounds demonstrated ability to specifically intervene in the complement cascade, for potentially prolonged periods of time, at what we believe to be the optimal point so that the disease-causing actions of complement proteins generally are inhibited while the normal disease-preventing functions of complement proteins generally remain intact as do other aspects of immune function.

Each of Cambridge Antibody Technology Group (a subsidiary of AstraZeneca PLC), Medarex, Amgen, Dyax Corporation, and MorphoSys AG has publicly announced intentions to develop therapeutic genetically altered human antibodies from libraries of human antibody genes. Additionally, each of Amgen, Inc., and Medarex, Inc. has publicly announced intentions to develop therapeutic genetically altered human antibodies from mice that have been bred to include some human antibody genes.

Employees

As of December 31, 2006, we had 296 full-time employees, of which 188 were engaged in research, development, manufacturing, and clinical development, and 108 in administration, commercial and business development and finance. Doctorates are held by 73 of our employees. Each of our employees is required to sign a confidentiality agreement. Our employees are not represented by any coll