



2008 Annual Report

Transforming Lives Through Innovation



## Mission Statement

Alexion Pharmaceuticals is a biopharmaceutical company working to develop and deliver life-changing drug therapies for patients with serious and life-threatening medical conditions, including hematologic diseases, cancer, and autoimmune disorders.



## Improving the Human Condition

In September 2008, Alexion's Soliris® (eculizumab) received the 2008 Prix Galien USA Award for Best Biotechnology Product, with Broad Implications for Future Biomedical Research. The Prix Galien recognizes the technical, scientific, and clinical research skills that were necessary to develop this innovative, first-in-class complement inhibitor, and the impact that Soliris is having on the lives of patients with paroxysmal nocturnal hemoglobinuria (PNH).

# 2008 Accomplishments

## January

- Dosing begins in AEGIS, an open-label registration study of Soliris® as a treatment for patients with PNH in Japan

## February

- Alexion acquires all rights to Oklahoma Medical Research Foundation patents related to Soliris and complement technology

## March

- Enrollment completed in AEGIS study
- In the first quarter of 2008, Alexion records its first quarterly net income on a non-GAAP basis

## June

- Results from clinical trials show that Soliris improved fatigue in patients with PNH, independent of changes in anemia, by controlling hemolysis, according to analyses of study data presented by clinical investigators at the Congress of the European Hematology Association
- In the second quarter of 2008, Alexion records its first quarterly net income on a GAAP basis

## August

- The U.S. Patent and Trademark Office issues a patent related to Alexion's anti-CD200 monoclonal antibody

## September

- Soliris, an innovative, first-in-class complement inhibitor, receives the 2008 Prix Galien USA Award for Best Biotechnology Product, with Broad Implications for Future Medical Research

## December

- Multiple presentations by physicians at the Annual Meeting of the American Society of Hematology (ASH) include:
  - First clinical experience with Soliris in treating patients with atypical Hemolytic Uremic Syndrome (aHUS) and Cold Agglutinin Disease (CAD)
  - Positive results from the AEGIS study, with Soliris achieving primary and secondary endpoints
  - New data showing that Soliris reduced thrombosis and inflammation, and decreased pulmonary hypertension, in studies of patients with PNH

## At Year-End

- Net sales of Soliris reach \$259.0 million in the first full year of commercialization
- Alexion records its first full year of profitability on both a GAAP and non-GAAP basis
- Pricing and reimbursement processes related to the launch of Soliris are completed in the five largest European markets
- Diagnostic initiatives in the U.S. are increasingly helping physicians reduce delays in the diagnosis and treatment of patients with PNH
- Alexion employees are based in 10 countries

## Early 2009

- Soliris is approved as a treatment for all patients with PNH in Canada (January) and Australia (February)
- Alexion's New Drug Application (NDA) for Soliris is submitted in Japan (March) after the drug is designated as an orphan drug (January)
- Case reports on Soliris as a treatment for patients with aHUS are published in the *New England Journal of Medicine*
- Clinical programs are proceeding with:
  - Four studies of Soliris as a treatment for patients with aHUS
  - An investigator-initiated study of Soliris as a treatment for kidney transplant patients at high risk of organ rejection
  - An investigator-initiated study of Soliris as a treatment for patients with dense deposit disease, a rare and severe kidney disorder
  - A randomized clinical study of Soliris as a treatment for patients with myasthenia gravis, a rare and severe neuromuscular disorder
  - An investigator-initiated study of Soliris as a treatment for patients with multifocal motor neuropathy, a rare and severe autoimmune disorder
  - A study of Alexion's anti-CD200 antibody as a treatment for patients with chronic lymphocytic leukemia (CLL)

## Dear Shareholders

In 2008, Alexion's first full year of product sales, we continued to advance our strategic plan and achieved strong results in both the ongoing global launch of Soliris and the continuing expansion of our research and development pipeline. As Soliris, our innovative complement-inhibitor therapy, transformed the lives of an increasing number of patients with paroxysmal nocturnal hemoglobinuria (PNH) in the United States and many European countries, we systematically strengthened and extended our efforts to develop and deliver life-changing drug therapies for patients with other debilitating and life-threatening diseases. With our goal of bringing Soliris to additional patients with PNH around the world, we continued to expand and develop our organization, creating and implementing innovative awareness and outreach programs. On the research front, working with leading physicians, we initiated extensive clinical development programs to study Soliris and other monoclonal antibodies for the treatment of patients who have other severe and rare disorders with few, if any, effective treatment options.

Several accomplishments in particular serve as measures of our success in 2008 – and point to our potential for continued growth in 2009 and beyond:

- As more physicians, patients, payors, and health authorities recognized the clinical benefits of Soliris, global product revenues for Soliris totaled \$259 million.
- Alexion achieved profitability for the first time in its 17-year history, enabling further investment directed at improving patient care in the PNH community, as well as research into therapies for the treatment of patients with other rare and serious diseases.
- In September, the scientific innovation and clinical research skills embodied in Soliris were recognized when Alexion received the 2008 Prix Galien USA Award for Best Biotechnology Product – one of the pharmaceutical industry's highest accolades.
- In the United States, physicians continued to identify patients who will benefit from treatment with Soliris.
- In Europe, Alexion completed successful reimbursement discussions with health authorities in the five largest countries, improving access to Soliris for patients with PNH.
- In Japan, researchers reported positive results from a clinical trial of Soliris in patients with PNH, providing data needed to seek Japanese regulatory approval.
- Physicians presented their initial clinical experience with Soliris in patients with other severe and rare diseases in which complement plays a key role.
- We started clinical trials of Alexion's anti-CD200 monoclonal antibody, the lead candidate in our oncology program, for patients with chronic lymphocytic leukemia (CLL).

### Serving Patients with PNH

PNH is a rare, debilitating, and life-threatening blood disorder defined by hemolysis, or the destruction of red blood cells. In patients with PNH, hemolysis results in serious and progressive clinical consequences; approximately one-third of patients do not survive more than five years from the date of their initial diagnosis.

Soliris, a first-in-class terminal complement inhibitor, was approved as a treatment for all patients with PNH by the U.S. Food and Drug Administration (FDA) and the European Commission (EC) in 2007. In early 2009, Soliris received marketing authorization from health authorities in Canada and Australia. All four jurisdictions reviewed and approved marketing applications for Soliris under priority review or accelerated assessment procedures, and all four designated Soliris as an orphan drug.

We believe that every patient with PNH who can benefit from Soliris should have access to Soliris. As part of our commitment to this objective, we are helping to increase awareness about PNH by providing vital information about the diagnosis, complications, and treatment of PNH to physicians, patients, and reimbursement authorities.

As we focus on meeting the needs of patients around the world during the ongoing global introduction of Soliris, we have aligned our operations into four territories: the Americas, Europe/Middle-East/Africa, Japan, and Asia-Pacific. Today, Soliris is being provided to patients in more than 18 countries across these territories, and we expect that its use as a treatment for patients with PNH will continue to increase significantly.

### The Americas

In 2008, we observed an increasing recognition among U.S. physicians of the debilitating, progressive and life-threatening nature of PNH. Physicians are engaging in increased activities to identify and diagnose patients suffering from the disease. Consequently, more patients suffering from PNH were identified, third-party payors continued to approve Soliris based on the patient's medical need and the judgment of the treating physician, and more patients were able to commence treatment with Soliris. Our observations reinforce our strategic imperatives including educating physicians about PNH, creating access, and supporting appropriate utilization.

In Canada, we are developing our commercial operations following the recent approval of Soliris. In 2009, we are working with Canadian healthcare organizations to provide access to Soliris as soon as possible.

We are also in the early stages of market entry in a group of Latin American nations, and could begin serving a small number of patients in one or more of these countries by the end of 2009. We expect to build our organization in Latin America throughout 2009 and 2010.

### Europe/Middle-East/Africa

In 2008, we were pleased to complete the pricing and reimbursement processes for the launch of Soliris in France, Germany, Italy, the Netherlands, Spain, and the United Kingdom, with England agreeing to fund Soliris for patients with PNH starting in April 2009. We appreciate that these and other European governments recognize the importance of access to Soliris for their citizens with PNH.

In 2009, given the robust reception for Soliris in the largest countries, we are broadening our commitment to patients across Europe in several ways. We are working with physicians to improve the awareness of PNH within both the medical and patient communities in European countries. We have established a European Union regional hub in Brussels to support our entry into additional countries on the continent. At the same time, we are greatly expanding our facilities in Lausanne, Switzerland, which will serve as our operational headquarters for the entire Europe/Middle-East/Africa region and will provide critical shared services to our markets outside North America.

### Japan

Our progress in bringing Soliris to patients in Japan, which gained much momentum in 2008, has continued into 2009. During 2008, enrollment and dosing in the AEGIS clinical study of Soliris as a treatment for Japanese patients with PNH were completed, and the markedly positive results of the trial were presented at the American Society of Hematology (ASH) 50th Annual Meeting in San Francisco in December. At ASH, we also met with more than 80 prominent Japanese



**Leonard Bell, M.D.**  
Chief Executive Officer

hematologists with research and clinical interest in PNH, an unusually large number for an "ultra-orphan" condition. In March 2009, we submitted our New Drug Application (NDA) for Soliris as a treatment for patients with PNH to the regulatory authorities in Japan. The orphan drug designation for Soliris, received in January 2009, entitles the NDA to priority review, which positions us potentially to begin commercial operations in Japan in late 2010.

#### Asia-Pacific

In February 2009, the Australian Therapeutic Goods Administration became the most recent regulatory authority to approve Soliris as a treatment for patients with PNH. With Australian approval, our Sydney-based organization is now working with the federal healthcare authorities to ensure broad access for patients with PNH who can benefit from the drug. A government decision regarding access for eligible patients to Soliris therapy is expected by the end of 2009, and our Australian organization is preparing for initial commercialization in that country in 2010, as well as developing market entry strategies for other Asian and Pacific nations.

#### Innovation and Access – Essential to Patients with Rare Disorders

As our global organization grows, we are able to apply the specialized drug-development and organizational skills we have developed to address the unique needs of patients with rare and ultra-rare diseases. We were proud to join the National Organization for Rare Disorders (NORD) in celebrating the 25th anniversary of the passage of the Orphan Drug Act (ODA) in the U.S. during 2008. The ODA provides essential support for the development of therapies for diseases that affect as few as several hundred patients. As Congress recognized when it enacted the ODA, orphan drug development requires a degree of scientific innovation and regulatory expertise – and a level of investment and risk of failure – equal to or greater than that associated with the development of drugs for diseases affecting millions of Americans. When innovative therapies do exist, patients with orphan diseases deserve access to them, which requires a range of coordinated, patient-centered efforts among drug developers, governmental and private healthcare organizations, and policy makers. Alexion is focused on acting for the benefit of underserved individuals afflicted by ultra-rare, complement-mediated disorders.

#### Operating Results

As a result of the strong performance of our operating units, we were able to provide Soliris to an increasing number of patients in each sequential quarter of 2008 in both the U.S. and Europe. We recorded 2008 global revenues of \$259.0 million from Soliris net product sales and reported Alexion's first profit in the 17 fiscal years since Alexion was established in 1992, achieving a GAAP net income of \$33.1 million, or \$0.39 per diluted share, for 2008, compared to a GAAP net loss of \$92.3 million, or \$1.27 per share, in 2007.

Of course, while it is an important milestone, this initial profit represents only a small portion of the more than \$800 million we invested during the many years before Soliris was approved. In addition, we are committed to further investment to serve more patients with PNH in



Vikas Sinha, M.B.A., C.A., CPA  
Senior Vice President and Chief Financial Officer  
*Joined Alexion in 2005*



more countries – while developing treatments for patients with other severe and rare disorders. As we pursue these imperatives in an uncertain global economic environment, we continue to maintain the same high level of fiscal discipline in our scientific and business activities that has enabled us to accomplish our objectives to date.

### PNH Research

In recent years, physicians and their patients with PNH have benefited greatly from a growing body of knowledge about the natural history of this rare and serious disease. In 2008, dedicated researchers around the world again added significantly to the scientific and clinical understanding of PNH. New data on the progressive and life-threatening characteristics of PNH were presented during the year at scientific conferences:

- According to data presented by clinical investigators in June at the European Hematology Association (EHA) 13th Annual Congress in Copenhagen, fatigue experienced by patients with PNH is related directly to hemolysis and can be improved in these patients independent of correction of anemia. These data from clinical trials showed that Soliris therapy improved the often disabling fatigue experienced by patients with PNH.
- In clinical data presented at the ASH meeting in December, researchers reported on their observations that patients with PNH, including those without prior transfusion or evidence of blood clot, had significant elevation in proteins associated with thrombosis and inflammation. Soliris significantly reduced the level of these thrombogenic proteins in studied patients. This research is consistent with clinical trial data that observed that PNH patients receiving Soliris experienced 92% fewer blood clots than prior to therapy.
- In another study presented at ASH, researchers reported that approximately 50% of studied patients with PNH have an elevated measure of serious pulmonary arterial

“We are committed to the objective that every patient with PNH who can benefit from Soliris will have access to Soliris.”

hypertension (PAH), which has been associated with increased mortality. Soliris was found to significantly reduce this same measure of PAH in these patients.

### The Prix Galien USA

In September, Alexion was honored with the 2008 Prix Galien USA Award for Best Biotechnology Product, with Broad Implications for Future Biomedical Research. The Award recognized the groundbreaking complement-inhibition technology of Soliris. The Prix Galien Award committee includes seven Nobel Laureates and is widely considered the pharmaceutical industry's highest accolade. We are deeply gratified by this honor.

### Soliris as a Treatment for Patients with Other Complement-Mediated Diseases

We believe that Soliris can play an important therapeutic role in treating patients suffering from other rare, debilitating, and life-threatening complement-mediated disorders for which treatment options are limited or nonexistent. Clinical research is currently underway in the following areas:

#### Nephrology

Atypical Hemolytic Uremic Syndrome (aHUS) is a rare disorder in which patients are deficient in normally occurring complement regulatory proteins, leading to chronic inflammation, hemolysis, and blood clots,

“With a growing international presence and the most robust pipeline in the company’s history, we have the opportunity and the responsibility to bring essential therapies to patients who have lived for too long without hope.”

ultimately resulting in kidney failure. Case reports on patients with aHUS treated with Soliris were presented at the ASH meeting and at the American Society of Nephrology (ASN) meeting in November 2008, and were published in January 2009 in the *New England Journal of Medicine*. These reports showed that Soliris reduced hemolysis and platelet consumption and improved kidney function in these patients. We are currently initiating four clinical trials of Soliris as a treatment for adult and adolescent patients with aHUS. These open-label prospective studies will be conducted at multiple sites worldwide, with enrollment and dosing expected to continue throughout 2009.

Also at ASN, positive initial clinical trial data were presented on the use of Soliris in kidney transplant patients at risk of severe antibody and complement-

mediated rejection. Patient enrollment continues in an investigator-initiated trial, and we are currently evaluating expansion of this program.

Initial patient dosing has also commenced in an investigator-initiated trial evaluating the use of Soliris as a treatment for patients with dense deposit disease (DDD), another rare and severe complement-mediated kidney disease.

#### Neurology

We are evaluating Soliris as a treatment for patients with two rare and severe complement-mediated neurodegenerative diseases:

- Patient enrollment is ongoing in our study of Soliris as a treatment for patients with myasthenia gravis, a rare disorder marked by debilitating and sometimes life-threatening weakness in key muscle groups.
- Dosing has commenced in a Phase II investigator-initiated study of Soliris in patients with multifocal motor neuropathy, a rare autoimmune disorder in which antibodies and complement attack the nervous system.

#### Hematology

Physicians reported a case study at the ASH meeting showing a positive clinical effect of Soliris treatment in a patient with cold agglutinin disease (CAD), another rare and life-threatening complement-mediated blood disorder. We anticipate evaluating with interested clinical investigators the use of Soliris in patients with this disease.

#### Oncology Program

The CD200 molecule, which is expressed at increased levels on the surface of several types of blood and solid tumors, acts to inhibit the normal immune response to tumor growth. Our anti-CD200 monoclonal antibody, the lead candidate in our oncology program, blocks CD200 and thus allows the immune system to then attack these tumors, and has been shown to reduce substantially the growth of aggressive human tumors in several model



systems. We are on track with enrollment and dosing in a study of our anti-CD200 monoclonal antibody as a treatment for patients with CLL. As we gain further knowledge, we plan to expand our anti-CD200 program to include patients with multiple myeloma.

### Manufacturing and Facilities

During 2008, we completed the engineering and validation runs required to commission our manufacturing facility in Smithfield, Rhode Island, which would provide us with a company-owned source of supply for clinical and commercial antibody products. We expect to file supplemental applications to both the FDA and European authorities in 2009, with the goal of manufacturing Soliris drug substance in Smithfield beginning in 2010.

In our Cheshire, Connecticut headquarters, we are continuing to drive toward a greener and more cost-effective energy footprint with efforts we hope to replicate elsewhere. In addition to retrofitting our lighting, cooling, heating, and control systems to substantially reduce our carbon footprint, we have now installed more than 1,700 solar panels to provide substantial amounts of zero-carbon electricity with negligible ongoing maintenance expenses.

### Senior Management Team

Upon his retirement in December, we offered our deepest thanks and best wishes to David Keiser, a co-founder of Alexion, the company's Chief Operating Officer since 1992 and President since 2002. David was instrumental in the robust introduction of Soliris in the United States and Europe, and helped to build a broad platform for global growth, which we are now driving under the leadership of Alexion's senior management team reporting to me: Stephen P. Squinto, Ph.D., Executive Vice President and Head of Research and Development; Patrice Coissac, SVP, and President of Alexion International Sàrl; Thomas I. H. Dubin, J.D., SVP and General Counsel; David L. Hallal, SVP, Commercial Operations, Americas; and Vikas Sinha, M.B.A., C.A., CPA, SVP and Chief Financial Officer.

### Looking Forward

Alexion's ability to combine scientific expertise with global commercial capability made 2008 another milestone year for patients with PNH and for Alexion. With a growing international presence and the most robust pipeline in the company's history, we have the opportunity and the responsibility to bring essential therapies to patients who have lived for too long without hope.

Of the few biotechnology companies that make the transition from drug development to commercial success, fewer still achieve the results and the momentum that we have attained. Our employees across all functions and territories deserve great credit for their patient-centered dedication. We are also grateful to the investors, researchers, practicing physicians, and patients themselves who have made our efforts possible. As we look toward the future, our commitment remains the same: to transform lives through innovation.



Leonard Bell, M.D.  
*Chief Executive Officer*

## Transforming Lives Through Innovation

“Our goal in every research program has been to translate basic science into life-changing treatments for patients who have severe and life-threatening diseases, and for whom safe and effective therapies do not exist. Soliris...is just such an accomplishment.”

Since Alexion was established in 1992, we have been committed to the innovation of breakthrough biopharmaceutical products. Our goal in every research program has been to translate basic science into life-changing treatments for patients who have severe and life-threatening diseases and for whom safe and effective therapies do not exist. Soliris, our first biologic product – discovered, developed, and delivered to physicians by Alexion employees – is just such an accomplishment. Soliris is the first terminal complement inhibitor and the first treatment, now approved in 33 countries, for patients with paroxysmal nocturnal hemoglobinuria (PNH). Soliris is also among the relatively small number of biologics being used as a safe and effective therapeutic for an ultra-rare disease.

### **PNH – A Complement Inhibitor Deficiency Disease**

PNH is a rare, debilitating and life-threatening genetic disease defined by hemolysis, the destruction of red blood cells. The hemolysis of PNH is caused by certain complement proteins of the patient's immune system directed against the patient's own blood cells. Although complement is an important part of the body's immune defenses, there are a number of “ultra-orphan” (extremely rare) diseases, including PNH, in which patients lack the complement inhibitors that normally protect healthy tissue from being attacked by complement. In PNH, this complement inhibitor deficiency develops without warning as a result of an acquired (non-hereditary) genetic mutation. The disease can occur in men and women of all races, backgrounds, and ages.

Hemolysis in patients with PNH is constant and sometimes silent, and can be life-threatening. In patients with PNH, hemolysis can cause blood clots, kidney disease, liver dysfunction, pulmonary hypertension, disabling fatigue, recurrent pain, impaired quality of life, shortness of breath, intermittent episodes of dark colored urine (hemoglobinuria), and anemia. From the time of diagnosis, the estimated median survival for patients with PNH is between 10 and 15 years, and one-third do not survive more than five years. It is estimated that only 8,000 to 10,000 people in the U.S. and Europe have PNH.

#### **Soliris – Personalized Medicine for Patients with PNH**

Soliris is transforming the lives of patients with PNH by preventing the chronic red blood cell destruction (hemolysis) that underlies the morbidities and mortality of the disease.

Complement is a series of proteins that are formed in a cascade, each one leading to the creation of the next. Soliris addresses hemolysis by targeted blocking of the complement cascade at the protein known as C5, the first element of the terminal portion of the cascade, without interfering with the vital immune functions of the earlier, or proximal, complement proteins. Every patient who received Soliris in our U.S. and European clinical trials experienced an objective response to the drug in the form of a reduction in hemolysis.

In addition to an immediate and sustained reduction in hemolysis, studied patients experienced significant improvements with regard to blood clots, kidney function, pulmonary hypertension, fatigue, transfusion requirements, anemia, and overall quality of life.

Significantly, clinical patients with PNH realized these benefits regardless of their symptoms, severity of disease, history of bone marrow failure, or transfusion needs prior to treatment.

Soliris was approved as the first treatment for all patients with PNH to prevent hemolysis by the U.S. Food and Drug Administration and the European Commission in 2007, and by Health Canada and Australia's Therapeutic Goods Administration in 2009. All four jurisdictions reviewed and approved their respective marketing applications for Soliris under their priority review or accelerated assessment procedures, and all four have designated



**Stephen P. Squinto, Ph.D.**  
Executive Vice President, Head of Research and Development  
*Joined Alexion in 1992*



“Soliris is transforming the lives of patients with PNH by preventing the chronic red blood cell destruction (hemolysis) that underlies the morbidities and mortality of their disease.”



Wendell Rosse, M.D. (far left), with the Alexion management team at the 2008 Prix Galien USA Award ceremony on September 24, 2008

Soliris as an orphan drug. Before Soliris, there were no therapies specifically available for patients with PNH. Treatment options were limited to symptom management through periodic blood transfusions, non-specific immunosuppressive therapy and, infrequently, bone marrow transplantations, a procedure that carries its own substantial risks of illness and death.

### **Expanding the Understanding of PNH**

Before the innovation of Soliris, patients with PNH suffered both from the clinical manifestations of their disease and from the lack of awareness and information surrounding it. In collaboration with the world's leading experts in PNH, we conducted one of the most extensive, multi-national, clinical research programs ever undertaken for an



ultra-orphan drug. In 2002, we performed a proof-in-principle study of eculizumab as a treatment for patients with PNH in the United Kingdom. The results from this successful trial were published in the *New England Journal of Medicine* in 2004, and were soon followed by two Phase III studies:

- TRIUMPH, a double-blind, randomized, placebo-controlled multi-center pivotal Phase III study, began in 2004 and was completed in 2005. Positive results were reported in January 2006 and published in the *New England Journal of Medicine* later that year.
- SHEPHERD, a 52-week open-label trial, began in 2005 and was completed in 2006. As in TRIUMPH, every patient treated with eculizumab in SHEPHERD responded with an objective reduction in hemolysis. These and other positive results were reported in late 2006 and published in the journal *Blood* in 2007.

Approximately 200 patients were enrolled in these studies, nearly all of whom took part in E05-001, a long-term extension study. Together, these studies provided the medical community with a more complete understanding of PNH and established the long-term efficacy and safety of Soliris therapy. Today, patients with PNH continue to benefit from the ongoing work of dedicated researchers:

- In data presented at the 50th Annual Meeting of the American Society of Hematology (ASH) in December 2008, clinical results showed that PNH study patients, most of whom did not have clinical evidence of thrombosis and were also not previously transfused, exhibited a hypercoagulable state as indicated by elevated levels of key inflammatory and pro-thrombotic measures. Soliris treatment was associated with significant reductions in these blood measures of coagulation in these PNH patients.

- In a separate study also presented at the ASH meeting, investigators reported data which indicated that approximately one-half of the studied PNH patients suffered from pulmonary hypertension, as measured by an elevated blood level of NT-proBNP, which has been shown to be highly predictive of pulmonary arterial hypertension (PAH) and an independent predictor of mortality in other hemolytic diseases. Soliris was observed to significantly reduce this indicator of PAH in the studied patients.
- Also at ASH, positive top-line results were reported from AEGIS, an open-label registration study examining Soliris as a treatment for Japanese patients with PNH. The pre-specified primary efficacy endpoint, reduction in hemolysis, was achieved with statistical significance, as were important secondary endpoints. Soliris appeared to be safe and well tolerated in AEGIS study patients.
- In June 2008, investigators reported clinical study data at the European Hematology Association (EHA) 13th Congress in Copenhagen showing that Soliris therapy improved the often disabling fatigue experienced by patients with PNH independent of improvements in anemia. This study indicated that patients may experience life-changing improvements in fatigue with long-term Soliris therapy regardless of changes in their anemia.

The successful innovation of Soliris and the ongoing studies in patients with PNH demonstrate the potential to transform the lives of the most underserved patients – those with diseases that are ultra-rare, little understood, and lacking therapies. Alexion is committed to the objective that every patient who can benefit from Soliris will have access to Soliris.



“Soliris addresses hemolysis by targeted blocking of the complement cascade at the protein known as C5, the first element of the terminal portion of the cascade, without interfering with the vital immune functions of the earlier, or proximal, complement proteins.”



Russell P. Rother, Ph.D.  
Senior Vice President and Chief Scientific Officer  
*Joined Alexion in 1992*

## Serving the PNH Community

Since Soliris was approved in the U.S. and European Union in 2007, patients with PNH have made significant strides toward better health. Today, as physicians attain a better understanding of the progressive nature and clinical consequences of the disease, patients with PNH in many countries have a higher likelihood for early and accurate diagnoses and more effective treatment.

Alexion supports the PNH community by working with researchers, physicians, advocacy organizations, third-party payors, public health officials – and, of course, patients and their families. Yet for all the progress to date, we know that, on a global basis, our journey toward improving patients' lives has just begun. We are committed to the objective that every patient with PNH who can benefit from Soliris will have access to Soliris, and we continue to support such access through multiple ongoing initiatives:

- Collaborating with dedicated researchers around the world as they learn more about PNH
- Educating physicians and patients on the progressive and life-threatening nature of PNH so they can make better-informed diagnostic and treatment decisions
- Creating access for all patients with PNH by supporting patient advocacy programs and offering patient services such as those provided by our OneSource™ Treatment Support Program in the U.S.
- Supporting appropriate utilization of Soliris through a global supply network that delivers Soliris when and where it is needed
- Seeking regulatory approvals in countries beyond the U.S. and European Union, and working with national healthcare authorities on details of providing access

### Disease Education and Awareness

Perhaps no area of support to the PNH community is more important than overcoming the low levels of disease knowledge and awareness surrounding PNH. This situation is all too common for patients who suffer from an ultra-rare disease, and is especially serious in the case of a progressive and life-threatening disease such as PNH. Through comprehensive disease education efforts, a growing number of physicians in the U.S. and Europe are becoming better able to identify patients who are at a greater likelihood of having PNH – either because they have disorders such as aplastic anemia or myelodysplastic syndromes, which are known to have higher rates of concomitance with PNH, or because they have clinical signs and symptoms, such as hemolytic anemia or unexplained blood clots, which can be caused by the disease. In the U.S., more physicians are responding to this increased understanding by testing such patients for the presence of PNH. Throughout 2008 and continuing into 2009, use of high quality diagnostic testing continued to increase in the U.S. We expect that educational initiatives will have a continued and growing



## “PNH turned my life upside down”

Maria, mother of two, PNH Patient

“I was 22 when I was diagnosed with PNH, and the disease turned my life upside down.

“At first, I thought my extreme fatigue, severe vomiting and constant body aches were part of being pregnant. But after the baby was born, and after a series of tests, I was eventually diagnosed with PNH. I was very scared because there was little information about the disease.

“At the time, my daughter was two years old and my son was a newborn. I was told that most people with PNH only live about 10 years. I was devastated and worried constantly about leaving my children and husband behind. I started getting blood transfusions every six months, but as the disease progressed I needed them every two to three weeks.

“I think back to my life before Soliris and the journey I have had living with PNH.

“There were several times that I almost died from the consequences of PNH. I had kidney failure, several blood clots – including a clot in my brain – and a stroke that left me in a coma.”

“After my stroke, I was temporarily paralyzed and had to re-learn how to eat, talk, brush my teeth and how to put on my shoes.

“I learned about Soliris after living with PNH for over 20 years. In May 2007 I started my first treatment. I got more energy and stopped having to go for blood transfusions every month, which was a huge milestone for me. Today, I go into the hospital every two weeks, get my Soliris treatment and then I come home. I can plan ahead, venture out into the world, and not worry as much about having another ‘episode’ caused by PNH.

“It is amazing to me and my family that my PNH is under control, and I am living an independent and normal life.

“Soliris has helped me manage my PNH. Today, we have the freedom to plan a vacation and spend time with our kids. But most importantly, I have hope that I will see both of my kids graduate from college, be at my daughter’s wedding, and my husband and I even dream of becoming grandparents.”





## “The patient comes first”

Paula Bonanni, R.N., M.B.A., Nurse Case Manager, *Joined Alexion in 2007*

“Every day, I have the privilege of helping people who are living with a rare and serious disorder called paroxysmal nocturnal hemoglobinuria, or PNH. My name is Paula Bonanni, and I’m an Alexion Nurse Case Manager in the OneSource program.

“I provide patients with information about the disease and its treatment. I draw on my nursing experience to provide the right mix of education, compassion and resources. I can even arrange for newly diagnosed patients to connect with others who have been living with the disease for a while to share their experiences.

“Patients and their families are grateful for our services, which include educating them about options for accessing treatment. This approach has helped patients to obtain timely, efficient and continuous access to therapy.

“For us, the patient always comes first. Our patients appreciate what we say and what we do, and often tell us so. This sense of purpose makes Alexion a great place to work.”

“People with rare disorders face many challenges, from securing an accurate diagnosis to understanding options for accessing treatment. When patients first receive a diagnosis of PNH, they often feel overwhelmed and alone. My job is to support patients every step of the way.”



impact to optimize the diagnosis and treatment of patients with PNH. Physicians in some European countries are also starting to test patients with a higher likelihood of having PNH.

### **Improved Laboratory Testing**

In response to increasing demand by hematologists and oncologists for more accurate PNH testing for their patients who might have PNH, a growing number of laboratories in the U.S. are providing high-sensitivity flow cytometry testing. We expect that, as more diagnostic labs improve their testing methods to meet physician demand, it will enable more patients to receive an accurate diagnosis without potentially dangerous delays.

### **Supporting Access in the U.S. Through OneSource™**

To meet the specific needs of patients receiving care within the healthcare system in the United States, Alexion created Soliris OneSource, a personalized treatment support service for patients with PNH and their healthcare providers. Each PNH patient is assigned to an Alexion Nurse Case Manager who will support the patient by providing a broad range of services from disease education to assisting with access solutions. All Alexion Case Managers are registered nurses who have extensive insurance and health care industry expertise.

We are pleased that in the United States patients have broad and efficient access to Soliris, based on the product's labeling and compelling clinical benefits. For patients whose insurance is not adequate, our Alexion Case Managers can help to identify alternative coverage or funding. In addition, the National Organization for Rare Disorders (NORD) has established the PNH Fund to assist underinsured patients. Finally, our Alexion Case Managers will make referrals to the COMPLEMENT Foundation for patients who do not have insurance, access to insurance, or any other means for obtaining Soliris.

### **Patient Advocacy**

In addition to our work with NORD in the U.S., Alexion supports patient advocacy groups in other countries. The European Organization for Rare Diseases (EURORDIS) is a non-governmental patient-driven alliance of patient organizations and individuals active in the field of rare diseases. EURORDIS is dedicated to improving the quality of life of people living with rare diseases in Europe and is the voice of the 30 million patients affected by rare diseases throughout the continent. As a member of the EURORDIS Roundtable of Companies, Alexion works with EURORDIS and the European rare disease community to improve patients' access to information, treatment, care, services, and support for people living with rare diseases across Europe.

ORPHANET is a public database of information on rare diseases and orphan drugs. Its aim is to improve diagnosis, care and treatment of patients with rare diseases. ORPHANET provides an expert-authored and peer-reviewed Professional Encyclopedia, a Patient Encyclopedia, and a Directory of Expert Services. Alexion Europe actively participates in ORPHANET initiatives, including, in 2008, the translation of ORPHANET rare disease emergency guidelines into five languages. Patients with rare diseases faced with a health emergency may frequently encounter emergency room professionals unfamiliar with their particular disorder and unsure of how to administer emergency services appropriately and safely. Translation of these guidelines helps emergency professionals throughout Europe to better manage their rare disease patients.

### **Expanding Patient Access to Additional Countries**

A key element of our commitment to the PNH community is to bring the life-transforming benefits of Soliris to patients with PNH in more countries. In early 2009, Soliris received marketing authorizations from Health Canada and Australia's Therapeutic Goods Administration, and we submitted our New Drug Application to the regulatory authorities in Japan. Soliris is now approved as a treatment for patients with PNH in 33 countries.

## Locations



- Soliris Approved for Marketing
- Marketing Application Under Review





## Supporting Access to Soliris Worldwide

In 2008, our first full year of commercial operations, Alexion completed its transformation into a commercially successful global biopharmaceutical company. Today, physicians are providing Soliris to their patients with PNH in more than 18 countries. To efficiently meet the fast-growing demand for Soliris, which includes providing substantial support and services on a patient-by-patient basis, we have aligned our expanding commercial operations into four territories: the Americas, Europe/Middle-East/Africa, Japan, and Asia-Pacific. Our employees in all countries facilitate patient access to Soliris through education on the diagnosis, natural history, and treatment of PNH, and work closely with physicians, private payors, and government reimbursement authorities, as appropriate, to help patients with PNH reduce the significant clinical consequences and life-threatening risks of their disease.



**David L. Hallal**

Senior Vice President, Commercial Operations, Americas

*Joined Alexion in 2006*

### Americas

The launch of Soliris in the U.S. has followed a steady trajectory since March of 2007, driven by our four commercial strategic imperatives: identifying patients diagnosed with PNH through physician education, educating physicians regarding the serious and progressive nature of PNH and the importance of treating patients with the disease, creating access to Soliris for all patients with PNH, and supporting appropriate utilization of Soliris. Our success in the U.S. has been a result of consistent execution of our plans to meet these imperatives.

As is the case in many rare and ultra-rare diseases, many patients with PNH suffer for years without an accurate diagnosis and as a result receive suboptimal treatment. Through our comprehensive disease education efforts, a growing number of U.S. physicians are better able to identify patients with PNH and treat them without delay. As we look to provide greater focus within our field teams on the education of both physicians in practice and hematopathologists in diagnostic laboratories, we expect these programs to have a continued and growing impact on the improved diagnosis and identification of patients with PNH.

Elsewhere in the Americas, Soliris was approved in January 2009 by Health Canada for all patients with PNH. We are beginning to work with Canadian public and private healthcare organizations so that they can provide access to Soliris for the first patients in that country later in 2009. We expect to serve an even larger number of patients in 2010.

We are also in the early stages of market entry in the first group of countries in Latin America and could begin serving a small number of patients in one or more of these nations by the end of 2009. We expect to build our organization in Latin America throughout 2009 and into 2010.

### Europe/Middle-East/Africa

In 2008, Alexion successfully completed the pricing and reimbursement processes for the launch of Soliris in the top five European markets – France, Germany, Italy, Spain, and England – as well as in The Netherlands. As a result, more patients in these and other countries were able to

obtain access to Soliris through their national healthcare systems in 2008.

In England, where many of the Soliris clinical trial patients were located, the National Health Service will begin national funding of Soliris therapy in April 2009, enabling these study patients to transition to commercial status and providing access for eligible patients in the future.

In 2009, our in-country organizations will continue to adapt our diagnostic education initiatives to local healthcare delivery systems while implementing expanded disease awareness initiatives describing the progressive and debilitating nature of PNH. We are also greatly expanding the role of our facility in Lausanne, Switzerland, which will now serve as the commercial headquarters for the Europe/Middle-East/Africa region while providing critical shared services to our markets outside of North America on a centralized, best-practices basis.

Our office in Brussels, opened in 2008, is also expanding, and will provide multi-country support in the smaller European markets. In each country, we have been fortunate in finding talented and experienced professionals with proven records of serving patients and their healthcare providers. Throughout 2009, Alexion will develop in-country operations in the next cluster of 10 to 15 EU nations, and we also expect to begin serving the needs of initial patients and physicians in countries of the Middle-East during the year.

### Japan

In March 2009, Alexion submitted a New Drug Application (NDA) for Soliris as a treatment for patients with PNH in Japan. Because the Japanese health authorities have already designated Soliris as an orphan drug, the NDA will receive priority review and, subsequent to approval, Soliris will have 10 years of market exclusivity as a treatment for patients with PNH. We are building out our Tokyo-based commercial organization in anticipation of a commercial launch of Soliris in that country in 2010. For several reasons, Japan presents an especially important opportunity to serve patients with PNH who have been suffering without a safe and effective

therapy. Much of the early research in PNH took place in Japan during the 1980s and '90s, and there is a high level of awareness among a large community of physicians and researchers in that country, as evidenced by the rapid enrollment and completion of our AEGIS study there.

### Asia-Pacific

Our most recent approval for Soliris was received from Australia's Therapeutic Goods Administration in February 2009. Our regional leadership team in Sydney is now working with the federal healthcare authorities to provide broad access to Soliris for patients with PNH who can benefit from the drug. A decision regarding reimbursement for eligible patients is expected by the end of 2009 and our Australian organization is preparing for initial commercialization in that country in 2010. Simultaneously, our Sydney team is developing strategies for market entry in other countries in Asia and the Pacific.



**Patrice Coissac**  
Senior Vice President, and President, Alexion International Sàrl  
*Joined Alexion in 2005*

## Working Together for Patients with Rare Diseases

“The hope for patients who have rare diseases but lack effective treatment is high-level scientific innovation, which often benefits broader groups of patients as well.”

More than 7,000 rare diseases have been identified; many are catastrophic, severe, chronic, and progressive, marked by pain, disability, degeneration, and high rates of mortality. Yet relatively few effective therapies exist for patients with these uncommon disorders.

The hope for patients who have rare diseases but lack effective treatment is high-level scientific innovation, which often benefits broader groups of patients as well. Indeed, while orphan drugs often represent the best examples of personalized medicines for patients with very rare genetic deficiencies, they also expand the frontiers of medicine in general. But the obstacles to this innovation are substantial. Because rare disorders are not studied to the same degree as more commonplace illnesses, knowledge is often limited, resulting in a paucity of both accurate diagnostics and effective therapies. These problems can be sharply compounded for patients with disorders that are ultra-rare: a term generally used for diseases with a prevalence of fewer than 20 patients per one million of population.

### Factors in Orphan Drug Innovation

Biopharmaceutical companies face unique challenges as they seek to innovate safe and effective therapies for patients with ultra-rare diseases. This is true even for companies like Alexion, which have successfully brought a drug for an ultra-rare disease to market. While all drug development is risky, it is especially so in uncommon disease states, often entailing greater drug development complexities and clinical uncertainties. These include the need to identify sufficient numbers of patients to participate in drug trials and the necessity of including a large number of study sites, in multiple countries, since each may be able to enroll just one or two patients. In addition, regulatory risk may be markedly increased for development of orphan drugs since there is usually no approved therapy for these diseases and no well-established roadmap to marketing approval. The relatively

small number of products that eventually receive approval necessarily requires that the burden of the failed development be incorporated into the costs of the few successfully developed products. Also, most orphan drugs are complex biologics (such as proteins) that require living cells for production, rather than chemical drugs whose production is typically simpler and less expensive. The costs, risks and difficulties of developing and manufacturing biological products typically exceed those for chemical products. Once an orphan drug is approved, the innovator typically engages in extensive post-marketing research, physician education, and patient support, as well as safety monitoring, which may also be more expensive for orphan drugs. Orphan drug companies often establish expensive lifetime patient registries to further monitor patients with these rare disorders, in order to ensure continued safety and to develop further medical knowledge.

These and other factors can combine to impact the costs, and thus the pricing, of an orphan drug, which in some cases will be used to treat only a few hundred patients.

#### **Public Policies to Support Innovation and Access**

Fortunately for patients with rare diseases, healthcare authorities in many countries have recognized the need to encourage therapeutic innovation – and, equally important, to support access to drug therapies once they are available. For example, the U.S. Orphan Drug Act (ODA), whose 25th anniversary was observed in 2008, provides important incentives, including seven years of market exclusivity, to companies that succeed in developing a treatment for a rare disease. The Regulation on Orphan Medicinal Products (ROMP), enacted by the European Parliament in 1999, creates similar incentives in the EU. These vital pieces of legislation have led to the development of more than 300 safe and effective therapies for patients with rare disorders, of which the approval of Soliris as a treatment for patients with PNH is

one example. Similar incentives exist in other countries, including Japan, where orphan drug designation provides for accelerated review of New Drug Applications and 10 years of market exclusivity upon approval.

The success of the ODA and similar legislation derives from the recognition that, despite the small number of treatable patients, orphan drug development entails a level of investment – and a risk of failure – equal to or greater than that associated with the development of drugs for diseases that affect millions. In any one country, and more so on a global basis, the job of helping patients who suffer from rare disorders has just begun. At Alexion, we are committed to working with private healthcare organizations, policy makers, and public health authorities so that patients with orphan diseases can have access to the innovative therapies that they deserve.



**Thomas I. H. Dubin, J.D.**  
Senior Vice President and General Counsel  
*Joined Alexion in 2001*



## Researching Severe and Rare Diseases

Beyond PNH, the safety and efficacy of Soliris as a first-in-class C5 complement inhibitor point to the strong potential of eculizumab – given intravenously or in other dosage forms – as a treatment for patients with other severe and rare complement-mediated diseases. These include disorders resulting from a deficiency in normally occurring complement inhibitors, as well as other conditions in which inappropriate or excessive complement activation plays a role. We believe that Soliris can provide life-transforming clinical benefits to patients with such conditions, and Alexion is committed to ongoing research investments toward this goal.

### Skill in Rare Disease R&D

Many complement-mediated diseases are rare or ultra-rare, which enables us to apply the skills we honed when we initially developed Soliris using internal resources at each step of the way, from the laboratory through regulatory approval. Among these capabilities is Alexion's expertise in conducting global clinical studies at multiple sites, many of which have just one or two patients, as well as the ability to work closely with an international network of scientists and to develop trial protocols in areas of medicine in which little prior research has taken place.

Our research programs further benefit from a growing synergy between our newer pipeline programs in complement-inhibitor deficiency disorders and the growing body of research in PNH. For example, the data on the importance of elevated blood measures of thrombosis and inflammation in PNH, presented in December 2008 at the ASH meeting, help us to better understand disease mechanisms common to other complement-inhibitor deficiency disorders.

Overall, our research and development pipeline is more robust than at any time in Alexion's history. In 2009, building on our success with Soliris and PNH, we expect to drive our Soliris franchise with at least eight clinical studies in five or more additional severe and rare complement-mediated disorders. At the same time, in our oncology program, we are continuing to study our anti-CD200

monoclonal antibody as a treatment for patients with chronic lymphocytic leukemia (CLL), and we are broadening this program to include patients with additional cancers.

### Kidney Disorders

Through a variety of mechanisms, complement plays a role in certain severe and life-threatening kidney diseases. Initial research leads investigators to believe that Soliris, as a terminal complement inhibitor, may provide a significant therapeutic impact to patients with these diseases, and we are currently focused on three such rare disorders.

#### Atypical Hemolytic Uremic Syndrome (aHUS)

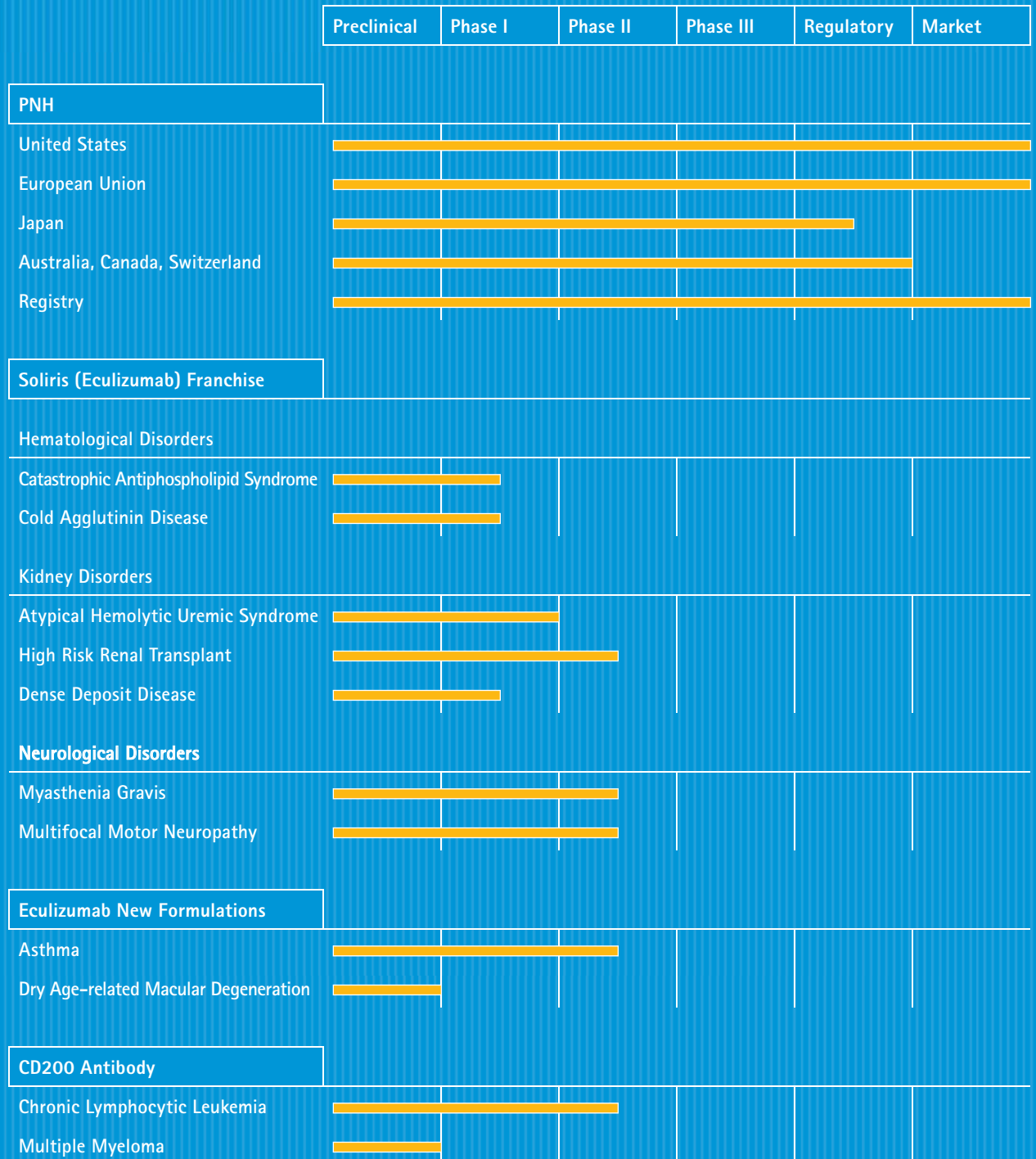
Like PNH, aHUS is an ultra-rare disorder in which patients are deficient in certain normally occurring complement inhibitors. In patients with aHUS, the insufficiency leads to chronic hemolysis, inflammation, and blood clots, resulting in kidney failure and shortened life. Typically, patients with aHUS have genetic mutations in one of several complement inhibitor proteins that lead to uncontrolled complement activation, which contributes to severe inflammation of the blood vessels and blood clotting. The prognosis for patients with aHUS is poor. Approximately 70% of patients with the most common mutation experience chronic renal insufficiency, chronic dialysis, or death within a year of the first clinical episode. Many patients are children.

Case reports by clinicians, presented at the American Society of Nephrology (ASN) and at the ASH meetings in 2008, and published in the *New England Journal of Medicine* in early 2009, showed that Soliris reduced hemolysis and platelet consumption, and also improved kidney function, in these patients with aHUS. Alexion has initiated four prospective, open-label clinical studies of Soliris as a treatment for adolescent and adult patients with aHUS in North America and multiple European countries. Enrollment and dosing in these studies are expected to continue throughout 2009.

#### High-Risk Transplant Rejection

Published works, including a study reported in the *Journal of Immunology* in 2007, have indicated that Soliris could

# Research Pipeline



help to prevent the rejection of donor kidney transplants in certain patients at high risk for transplant rejection – those who are presensitized as a result of having high levels of antibodies that specifically react with the donated organ. The anti-T-cell therapies normally used to prevent kidney rejection are generally not effective against this rejection mechanism. In 2008, an investigator-initiated trial commenced, evaluating the use of Soliris as a treatment for these transplant patients. Positive initial data from this trial were presented at the 2008 ASN meeting, and patient enrollment continues in this study. We are currently evaluating expansion of this program.

#### Dense Deposit Disease (DDD)

Dense deposit disease, or Membranoproliferative Glomerulonephritis Type II, is a rare, genetic, complement-mediated kidney disorder characterized by deposits of complement-related materials in the filtering mechanisms

(glomeruli) of the kidney. This in turn leads to a thickening of capillary walls within the kidney and reduced kidney function. DDD occurs most frequently in children 15 years of age or younger, and approximately 50% of patients develop end-stage renal disease within 10 years of diagnosis. Initial patient dosing has begun in an investigator-initiated trial evaluating the use of Soliris as a treatment for patients with DDD.

#### Autoimmune Neurodegenerative Diseases

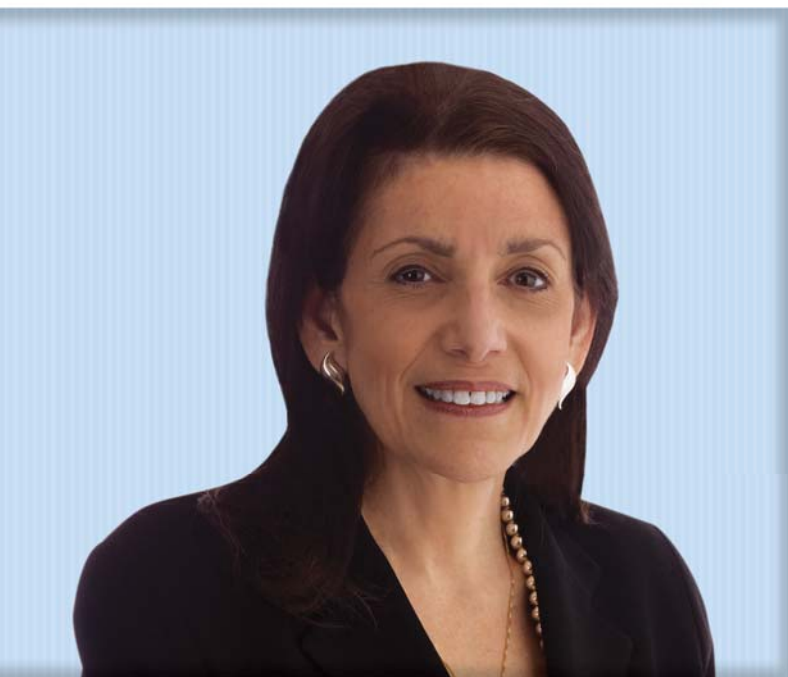
It has long been recognized that the inflammatory effects of terminal complement can interfere with or destroy certain mechanisms and structures of the nervous system. Investigation of Soliris as a treatment for patients with two rare and serious neurodegenerative diseases will continue through 2009.

#### Myasthenia Gravis

In normal muscular function, attachment of acetylcholine to receptors on the muscle side of the neuromuscular junction is a key part of the process that normally causes the muscle to contract. Some patients with myasthenia gravis generate autoantibodies against the acetylcholine receptor, which can activate terminal complement on the muscle side of the neuromuscular junction, resulting in increased failure of neuromuscular transmission. The resulting damage can lead to progressive symptoms that include slurred speech, difficulty in chewing or swallowing, weakness in the arms and legs, and difficulty in breathing, with approximately 10% of cases progressing to life-threatening failure of the respiratory muscles. A study, published in the *Journal of Immunology* in 2007, demonstrated the preclinical effectiveness of anti-C5 therapy in blocking this process in an animal model. Patient enrollment is ongoing in our study of Soliris as a treatment for these patients.

#### Multifocal Motor Neuropathy (MMN)

Terminal complement has been localized to nerve cells in MMN, and complement-mediated nerve and muscle damage have been demonstrated. The potential utility of an anti-C5 antibody has been demonstrated in a preclinical model of this disease. Data from the model, published in a 2008 issue



Camille L. Bedrosian, M.D.  
Senior Vice President and Chief Medical Officer  
Joined Alexion in 2008

of the journal *Brain*, showed that terminal complement is pathogenic in the nerve tissues and that inhibition with an anti-C5 antibody prevented complement-mediated nerve damage. In addition, measurements of neuropathy were markedly improved. Dosing has begun in a Phase II investigator-initiated study of Soliris in patients with MMN.

### Autoimmune Hemolytic Disorders

#### Cold Agglutinin Disease (CAD)

In the area of autoimmune hemolytic disorders, a case study was reported at the 2008 ASH meeting showing a positive clinical effect of Soliris in a patient with CAD, another rare and life-threatening complement-mediated blood disorder. We anticipate evaluating the use of Soliris in this disease with interested clinical investigators.

### Oncology Program

#### New Biologic Entity – Anti-CD200 Monoclonal Antibody

In addition to our work with Soliris and complement-mediated diseases, we are developing our proprietary anti-CD200 humanized monoclonal antibody. The molecule known as CD200 has been shown to be upregulated on tumors from patients with several cancers, including CLL, multiple myeloma (MM), melanoma, ovarian cancer, and neuroblastoma. CD200 is believed to interfere with the body's immune response to such tumors, a mechanism which may be essential to tumor growth and survival. Indeed, in patients with CLL and MM, the presence of the CD200 molecule on tumors is a negative prognostic indicator.

Scientific data show that our anti-CD200 monoclonal antibody blocks binding of CD200 to the CD200 receptor, which has been shown to enhance the immune response to tumors in preclinical studies. We have demonstrated the potent anti-tumor activity of our anti-CD200 antibody in a preclinical model of CLL, which was published in the January 2008 issue of the *Journal of Immunology*. Alexion is committed to investigating the therapeutic potential of our anti-CD200 antibody, beginning with an investigation of the molecule as a drug therapy for patients with B-cell CLL. CLL is the second most common type of leukemia in adults;

the American Cancer Society estimates that there were approximately 15,000 new cases of CLL in the United States in 2008, with approximately 4,000 people expected to die from the disease. Alexion is on track with patient enrollment and dosing of our anti-CD200 antibody in patients with CLL and is extending the investigation to patients with MM.

### Other Formulations of Eculizumab

Soliris is administered intravenously as a treatment for PNH. We are studying the potential of other dosage forms and routes of administration for eculizumab as treatments for patients with other complement-mediated diseases. In the fourth quarter of 2008, we completed dosing in our Phase II proof-of-concept trial of intravenous eculizumab as a treatment for patients with asthma. We expect that investigators will present data from this clinical study during 2009, and we may consider further studies in asthma with a nebulized form of the drug.



**Claude Nicaise, M.D.**  
Senior Vice President, Strategic Development and Global Regulatory  
*Joined Alexion in 2008*



## Selected Financial Highlights

Year Ended December 31,	2008	2007	2006
<b>Revenues:</b>			
Net product sales	\$ 259,004	\$ 66,381	\$ —
Contract research revenue	95	5,660	1,558
Total revenues	259,099	72,041	1,558
Cost of sales	28,366	6,696	—
<b>Operating Expenses:</b>			
Research and development	62,581	68,961	83,225
Selling, general and administrative	133,543	96,142	55,418
Total operating expenses	196,124	165,103	138,643
Operating income (loss)	34,609	(99,758)	(137,085)
Other income and expense	121	6,723	5,198
Income tax provision (benefit)	1,581	(745)	(373)
Net income (loss)	\$ 33,149	\$ (92,290)	\$ (131,514)
Earnings (loss) per common share			
Basic	\$ 0.43	\$ (1.27)	\$ (2.07)
Diluted	\$ 0.39	\$ (1.27)	\$ (2.07)
Shares used in computing earnings (loss) per share			
Basic	77,680	72,622	63,402
Diluted	89,967	72,622	63,402

At December 31,	2008	2007	2006
<b>Consolidated Balance Sheet Data:</b>			
Cash, cash equivalents, restricted cash, and marketable securities	\$ 139,711	\$ 106,712	\$ 250,148
Trade accounts receivable	74,476	46,278	—
Inventories	49,821	32,907	2,314
Total current assets	277,101	204,417	236,776
Property, plant and equipment	139,885	104,280	39,135
Total assets	477,551	334,357	333,537
Mortgage loan	44,000	44,000	26,000
Convertible subordinated notes	97,222	150,000	150,000
Total stockholders' equity	247,001	101,556	124,677

This annual report to shareholders contains forward-looking statements relating to our business, including information relating to our research, development, regulatory and commercial operations, the medical risks, benefits, regulatory and commercial potential of Soliris for PNH and other disorders and potential other drug candidates, as well as our financial information and prospects. Statements contained in this annual report 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. You should review the risks set forth from time to time in Alexion's filings with the Securities and Exchange Commission, including but not limited to the risks discussed in Alexion's Annual Report on Form 10-K for the period ended December 31, 2008. Alexion does not intend to update any of these forward-looking statements to reflect events or circumstances after the date of this annual report, except when a duty arises under law.

# Shareholder Information

## Directors

**Max Link, Ph.D.**<sup>1,4</sup>

Chairman of the Board;

Former Chairman of the Board  
and CEO, Centerpulse AG;

Former CEO, Corange;

Former Chairman of the Board  
and CEO, Sandoz Pharma, Ltd.

**Leonard Bell, M.D.**

Chief Executive Officer

**David W. Keiser**

Former President and  
Chief Operating Officer,  
Alexion Pharmaceuticals, Inc.

**Joseph A. Madri, Ph.D., M.D.**<sup>2,4</sup>

Professor of Pathology,  
Yale University School of Medicine

**Larry L. Mathis**<sup>1,3</sup>

Executive Consultant,  
D. Peterson Associates;  
Former President and CEO,  
The Methodist Hospital System

**R. Douglas Norby**<sup>1,3</sup>

Former Senior Vice President,  
Chief Financial Officer, Tessera, Inc.

**Alvin S. Parven**<sup>2,3</sup>

President, ASP Associates;  
Former Vice President,  
Aetna Health Plans

**Ruedi E. Waeger, Ph.D.**<sup>2,4</sup>

Former President and CEO,  
Aventis Behring L.L.C.;

Former President and CEO,  
ZLB Central Laboratories

## Senior Management

**Leonard Bell, M.D.**

Chief Executive Officer

**Stephen P. Squinto, Ph.D.**

Executive Vice President,  
Head of Research and Development

**Patrice Coissac**

Senior Vice President,  
President, Alexion International Sàrl

**Thomas I. H. Dubin, J.D.**

Senior Vice President  
and General Counsel

**David L. Hallal**

Senior Vice President,  
Commercial Operations, Americas

**Vikas Sinha, M.B.A., C.A., CPA**

Senior Vice President  
and Chief Financial Officer

**Camille L. Bedrosian, M.D.**

Senior Vice President  
and Chief Medical Officer

**M. Stacy Hooks, Ph.D.**

Senior Vice President,  
Technical Operations

**Claude Nicaise, M.D.**

Senior Vice President,  
Strategic Development and  
Global Regulatory

**Russell P. Rother, Ph.D.**

Senior Vice President  
and Chief Scientific Officer

**James P. Bilotta, M.B.A.**

Vice President  
and Chief Information Officer

**Daniel N. Caron**

Vice President,  
Site Operations and Engineering

**Glenn Melrose**

Vice President, Human Resources

**Jeremy P. Springhorn, Ph.D.**

Vice President, Corporate Strategy  
and Business Development

## Annual Shareholders Meeting

To be held on May 13, 2009

10:00 a.m. at the

Waterbury Holiday Inn

3580 East Main Street

Waterbury, CT 06705 USA

tel 203.706.1000

fax 203.755.1555

## Other Information

### Corporate Headquarters

Alexion Pharmaceuticals, Inc.

352 Knotter Drive

Cheshire, CT 06410

tel 203.272.2596

fax 203.271.8190

### Transfer Agent and Registrar

Continental Stock Transfer

& Trust Company

17 Battery Place

New York, NY 10004

### Investor Relations

Rx Communications

445 Park Avenue, 10th Floor

New York, NY 10022

tel 917.322.2569

fax 917.322.2570

### Media Relations

Makovsky + Company, Inc.

16 E. 34th Street, 15th Floor

New York, NY 10016

tel 212.508.9600

fax 212.751.9710

### Legal Counsel

Ropes & Gray LLP

Boston, MA

### Independent Auditors

PricewaterhouseCoopers LLP

Hartford, CT

### Trading Symbol

Listing for Alexion Pharmaceuticals

is found on the Nasdaq stock

market under the symbol ALXN.

[www.alexionpharma.com](http://www.alexionpharma.com)

<sup>1</sup> Member of Audit Committee

<sup>2</sup> Member of Compensation Committee

<sup>3</sup> Member of Nominating and  
Governance Committee

<sup>4</sup> Member of Compliance and  
Quality Committee

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## The Prix Galien

In September 2008, Alexion's Soliris® (eculizumab) received the 2008 Prix Galien USA Award for Best Biotechnology Product, with Broad Implications for Future Biomedical Research.



Alexion Pharmaceuticals, Inc. 352 Knotter Drive, Cheshire, CT 06410, USA  
Alexion International Sàrl Avenue du Tribunal Fédéral 34, 1005 Lausanne, Switzerland  
Alexion Europe SAS 25 Boulevard de l'Amiral Bruix, 75016, Paris, France  
Alexion Pharma K.K. Ebisu Prime Square Tower, Tokyo 150-0012, Japan  
Alexion Pharmaceuticals Australasia Pty Limited Brookvale NSW Australia, 2100  
[www.alexionpharma.com](http://www.alexionpharma.com)

