# To Our Shareholders:

In 2014, Alexion continued to expand its commercial and clinical operations as we advanced our mission to develop and deliver life-transforming therapies for patients with severe and life-threatening rare diseases. During the year, we reached a wide range of significant milestones on behalf of patients and their families while continuing to build a larger and highly efficient global enterprise to support a broad portfolio of transformative therapies, starting with our next product, asfotase alfa. Among our achievements in 2014, we:

- Continued to provide Soliris® (eculizumab) to an increasing number of patients worldwide with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS).
- Completed the rolling submission of our US Biologics License Application (BLA) for asfotase alfa as a treatment for patients with infantile- and juvenile-onset hypophosphatasia (HPP), a severe metabolic disorder, which the US Food and Drug Administration (FDA) has accepted for priority review. In addition, we completed our submissions for marketing authorizations for this highly innovative therapy in the EU and Japan, and we have significantly expanded the body of knowledge about HPP and the clinical benefits of asfotase alfa to support optimal patient care.
- Advanced the first two of our next-generation Soliris molecules into the clinic, and — based on initial clinical data — now intend to advance at least one of these molecules into Phase 2 trials in patients with PNH in 2015.
- Progressed our other key clinical development programs while establishing a strong foundation for future growth with an additional 17 preclinical development programs spanning diverse modalities and therapeutic areas.

## Reaching Patients with PNH and aHUS

We developed Soliris, the world's first and only approved terminal complement inhibitor, from the laboratory through regulatory approvals and commercialization in PNH and aHUS, two devastating and life-threatening ultra-rare disorders.

### PNH — Reaching More Patients Across our 50-Country Platform

The steady increase in the number of new patients starting on Soliris in 2014 affirms our view that, on a global basis, the majority of patients with PNH have yet to receive an accurate diagnosis, let alone commence appropriate therapy. Throughout 2014, as in prior years, we continued to identify a consistently high number of newly diagnosed patients with PNH in the US, Western Europe and Japan — the territories in which we have operated the longest — and we are also observing consistent additions of new patients commencing Soliris therapy across Turkey, Brazil and Russia. While we are pleased with the continued positive impact we are having on the lives of patients with PNH, we know that ongoing education is required to further enhance rapid and accurate diagnosis and effective treatment.

### aHUS — Strong Performance in the Ongoing Global Launch

We continued to observe a steady addition of new patients with aHUS commencing Soliris therapy in the US and Europe in 2014, while we made important progress in the early stages of serving patients with aHUS in Japan. The number of new patients with aHUS being identified by physicians — including

children who have rapidly progressing, life-threatening complications — confirms our view that our opportunity to serve patients and families suffering with aHUS is at least as large as our opportunity to serve the PNH community, and perhaps larger. As one measure, in the US — more than three years following their respective FDA approvals — more patients are currently receiving Soliris for aHUS than there had been for PNH. In Europe, we are experiencing a similar trend among patients with aHUS. These observations are in line with our view that the incidence of aHUS is likely higher than PNH. Our educational initiatives in aHUS are supported by the strengthening of our Soliris labels in the US and Europe, which now specify the important longer-term clinical benefits associated with chronic and sustained Soliris treatment with inclusion of results from two years of ongoing treatment.

## Advancing Our Relentless Mission to Provide Transformative Therapies

Beyond PNH and aHUS, we made significant progress across all of our lead development programs in 2014, all of which are focused on first-in-class therapeutic breakthroughs.

### Preparing for the Launch of Asfotase Alfa

As we prepare to provide our next product, asfotase alfa, to patients with HPP, we are applying key learnings from our experience in serving patients with PNH and aHUS for optimizing care with a highly innovative ultra-orphan therapy. We expect regulatory decisions in the US, EU and Japan this year, and are preparing to serve patients in the US and Germany during the first half of 2015 and in Japan by year-end. We are working with regulatory authorities to obtain these marketing authorizations as quickly as possible, given the high rates of mortality, severe debilitating effects and current lack of any approved therapy for patients with HPP.

In HPP, as in other ultra-rare disorders, education will be critical to helping patients, and our programs will employ the growing body of clinical data reflecting the potentially transformative impact of asfotase alfa. For example, researchers at the Endocrine Society Annual Meeting in March 2015 presented new data from a retrospective, multinational natural history study of children with HPP. Data from this study, which included 32 patients with juvenile-onset HPP, demonstrated that children with HPP have a substantial disease burden, particularly with regard to musculoskeletal abnormalities and growth deficiencies. These patients experienced HPP-related disease complications and morbidity that persisted despite standard efforts to control symptoms.

In parallel to the regulatory filings, we continue to build out our initial field-based medical teams and our in-country metabolic commercial teams, and they have begun educating physicians on the signs and symptoms of HPP and the appropriate pathways for a rapid and accurate diagnosis.

### Eculizumab: Expanding Our Portfolio with New Indications

As we seek to build on the strong, long-term safety and efficacy profile of Soliris® in PNH and aHUS, we are investigating eculizumab as a potential treatment for patients with other severe and rare complement-mediated disorders.

In neurology, we have development programs with eculizumab in patients with two severe disorders: neuromyelitis optica (NMO) and myasthenia gravis (MG). In 2014, we were pleased that eculizumab was

granted orphan drug designations in Japan for NMO and in the US, EU and Japan for MG. NMO is a life-threatening ultra-rare neurological disorder in which uncontrolled complement activation leads to severe damage to the central nervous system in patients, including their spinal cord and optic nerve. Our study is focused on patients who continue to experience relapses despite supportive treatment. Enrollment and dosing are ongoing in the PREVENT study, our registration trial in relapsing NMO.

MG is a debilitating and potentially life-threatening disorder in which uncontrolled complement activation results in destruction and inflammation at the junction between nerves and muscles in patients, leaving their muscles severely weakened. The REGAIN study, our registration trial in MG, is focused on patients with severe disease who are refractory to other treatment options. We expect to complete enrollment in REGAIN in 2015.

In transplant, a multinational registration trial with eculizumab in kidney transplant patients at increased risk for delayed graft function (DGF) is ongoing, and we expect to complete enrollment by the end of the year. DGF is an early and serious complication of organ transplantation that is characterized by the failure of a transplanted organ to function normally immediately following transplantation, potentially resulting in the loss of the organ. There is currently no approved therapy to prevent DGF in kidney transplant recipients. In addition, a significant number of donor kidneys are reportedly discarded each year due to the risk of DGF and its associated poor clinical outcomes.

We are also evaluating eculizumab in antibody-mediated rejection (AMR), a severe and potentially life-threatening condition that can lead to rapid deterioration of function and possible loss of the transplanted organ. Later this year we expect data from our Phase 2 deceased-donor study for the prevention of AMR, as well as the initiation of our clinical study with eculizumab for the treatment of patients with AMR. We continue to evaluate the results of our clinical study with eculizumab for the prevention of AMR in patients receiving living-donor transplants, which missed its primary endpoint.

### Other Highly Innovative Therapeutic Candidates

As the leaders in complement biology, we advanced the development of the first two next-generation Soliris® molecules in 2014. We initiated Phase I studies of ALXN1210 and ALXN5500, with additional molecules and programs in our expanding portfolio at earlier stages of development. The data already support advancing both of these molecules into further trials — and we intend to progress at least one of them into a Phase 2 PNH trial this year — with additional indications likely to follow. ALXN1210 is a longer-acting anti-C5 monoclonal antibody suitable for once-monthly dosing. We are targeting approval of at least one next-generation candidate in 2018.

We also have lead development programs with two additional highly innovative therapies, ALXN1007 and cyclic pyranopterin monophosphate (cPMP).

We have commenced dosing in two Phase 2 proof-of-concept studies to evaluate the safety and tolerability of ALXN1007 in patients with two severe and potentially life-threatening auto-immune diseases: graft-versus-host disease involving the gastrointestinal tract, or GI-GVHD, and antiphospholipid syndrome, or APS. We expect to have interim data in the GI-GVHD study later in 2015.

In our metabolic disease area, we continue to advance development of our cPMP replacement therapy for the treatment of patients with molybdenum cofactor deficiency (MoCD) Type A, a severe and life-threatening, ultra-rare, genetic metabolic disorder that causes catastrophic and irreversible neurologic damage within the first weeks of life. The synthetic cPMP bridging study in patients with MoCD is ongoing, and we expect to complete enrollment in 2015. We are also continuing our retrospective data collection and natural history study.

## Expanding Early-Stage Research

Within our portfolio of 17 preclinical programs, we have initiated preclinical development in our first seven messenger RNA (mRNA) programs with our collaborator Moderna Therapeutics, focused on the treatment of patients with severe and rare disorders. We are targeting our first candidate to enter the clinic in 2016. In addition, we entered into several other earlier-stage preclinical programs during 2014.

## Strong Financial Performance

2014 was another year of robust growth and profitability for Alexion as we provided Soliris to an increasing number of patients with PNH and aHUS worldwide. Net product sales for the year increased 44 percent to $2.234 billion, compared to $1.551 billion in 2013. Excluding the impact of $88 million for reimbursement of prior year shipments, 2014 net product sales increased 38 percent to $2.146 billion. By exceeding our revenue target, while maintaining strict financial discipline in our growing commercial and clinical activities, we reported 2014 non-GAAP EPS of $5.21 per diluted share, an increase of 69% year-over-year. Excluding the impact of the $88 million in pre-2014 sales, EPS would be $4.84, an increase of 57% in 2014. Our year-on-year revenue growth was robust across all territories we serve.

During 2014, we further aligned our global structure and invested in improving operational efficiency as we provide more therapies to more patients around the world. We expanded our Global Supply Chain and Quality operations in Ireland, which will include our first company-owned fill/finish facility. We are also in the process of moving our EMEA headquarters to Zurich, a major center for the pharmaceutical and biotechnology industries, to maximize our ability to attract talent and engage in commercial and academic collaborations. Finally, we have announced the establishment of the Alexion Research and Development Center in Paris, the first Alexion research facility outside of North America, which will focus on the discovery of innovative therapies for patients with severe, rare diseases.

## Recognizing Two Alexion Leaders

Along with our accomplishments in 2014, we were greatly saddened by the unexpected passing of Max Link, PhD, in October. Max had been a Director of Alexion since we were established in 1992, and served as Chairman of our Board of Directors since 2002. Please see page 2 herein to learn more about Max — an amazing person, a great friend and mentor, and one of our industry's leading champions of innovation for the benefit of patients.

Also in late 2014, Steve Squinto, PhD, my Alexion co-founder and friend, announced his planned retirement from Alexion effective January 1, 2015, following 22 years during which he helped to drive

Alexion's evolution into a global leader in the development, manufacturing and delivery of biotechnology therapeutics. We are very pleased that Steve will continue to contribute to our mission as the Chair of our newly established Scientific Advisory Board, and likewise pleased that Julie O'Neill has now taken on Steve's most recent position as Executive Vice President, Global Operations.

## Looking Ahead

In January 2015, we also announced my own retirement as CEO and the appointment of David Hallal, Alexion's Chief Operating Officer, as my successor, effective April 1, 2015. As Alexion is at a position of great strength with regard to commercial execution, financial discipline, and pipeline breadth and growth, the time is right for the Company, for David and for me personally to make this transition. In line with the thoughtful succession planning process undertaken by our Board, David will become the second CEO in our company's history. David has demonstrated outstanding leadership over the past decade at Alexion and has been instrumental in driving our results and building the high-performing, patient-centered culture for which we are known, with accomplishments that include leadership of the highly successful launches of Soliris® for PNH and aHUS and a key role in the build-out of our 50-country operating platform. As we have worked closely together for nearly a decade and increasingly shared responsibilities over the past few years, I know that David is the right person to lead us into our next chapter of growth, and I look forward to continuing to guide the Board and advising the Company on strategic matters in my role as Chairman.

For all that the Alexion team has accomplished for patients to date, we are excited that the opportunities ahead of us are far greater. In 2015 and beyond, our goals are to focus our global skills and resources toward serving a continuously increasing number of patients with PNH and aHUS … beginning to serve patients with HPP … and significantly expanding our portfolio through both internally and externally developed therapeutic candidates to provide transformative outcomes to patients suffering with severe and rare disorders.

As always, we thank our growing number of employees and the many other people who make our work possible — including researchers, physicians, patients and families. We are united in our commitment to serve patients with severe and life-threatening disorders through breakthrough medical innovation and to transform their lives from illness and desperation … into health and hope.

**Leonard Bell, MD**
*Chairman and Chief Executive Officer*

March 2015