Hemolysis Is Associated with Increased Mortality and Thrombosis in Patients with PNH

Additional Patient Registry Data Presented at ASH Annual Meeting Examined Burden of PNH on Patients' Lives

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) today announced the presentation of an analysis from the National Data Registry in South Korea that evaluated the association between hemolysis and mortality in patients with paroxysmal nocturnal hemoglobinuria (PNH). Researchers also presented new data from the PNH Registry, a multi-center, multi-national, observational study of patients with PNH: one presentation examined patient-reported quality of life, hospitalizations, and missed work, while a second evaluated the incidence of blood transfusions in patients with and without bone marrow disorders (BMD). Researchers reported these results at the 52nd American Society of Hematology (ASH) Annual Meeting and Exposition in Orlando.

PNH is an ultra-rare, life-threatening blood disorder in which chronic uncontrolled activation of the complement system causes the chronic destruction of red blood cells (hemolysis). Alexion is the maker of Soliris® (eculizumab), a first-in-class terminal complement inhibitor that is the first treatment developed specifically for PNH.

Elevated Hemolysis Associated With Early Mortality and Risk of Thrombosis

Researchers presented a poster titled, "Association Between Elevated Hemolysis at Diagnosis and Early Mortality and Risk of Thrombosis In Paroxysmal Nocturnal Hemoglobinuria (PNH) Patients with Cytopenia." (1) The analysis, which included 301 PNH patients from the National Data Registry in South Korea, evaluated the presence of hemolysis and cytopenia at the time of diagnosis and subsequent patient outcomes.

Researchers concluded that PNH patients with hemolysis are at an increased risk of mortality and life-threatening complications, and that hemolysis is a potential risk factor for mortality and life-threatening complications independent of the presence of cytopenia. In PNH patients with elevated hemolysis, as measured by lactate dehydrogenase (LDH) levels, researchers reported significantly higher rates of mortality (16% vs. 4%; p=0.019), thromboembolism (TE) (25% vs. 4%; p=0.001), and abdominal pain (54% vs. 32%; p=0.006) compared to PNH patients without hemolysis. In PNH patients with cytopenia, rates of mortality (19% vs. 3%; p=0.032), TE (19% vs. 3%; p=0.032), and abdominal pain (58% vs. 32%; p=0.015) also were significantly higher in patients with hemolysis compared to those without hemolysis.

"This research provides further evidence that uncontrolled complement activation and the resulting chronic hemolysis are the underlying causes of the morbidities and mortality associated with PNH," said Leonard Bell, M.D., Chief Executive Officer of Alexion.

The PNH Registry: Burden of Disease from Patient Perspective

In a poster session on Saturday titled, "Evaluation of Paroxysmal Nocturnal Hemoglobinuria Disease Burden: The Patient's Perspective," researchers presented patient-reported quality-of-life, hospitalization, and missed work outcomes for 431 patients enrolled in the PNH Registry. Patients were from 102 clinical sites in 17 countries and had completed a baseline questionnaire. (2)

In the study, patients with PNH reported a reduced quality of life as measured by the EORTC QLQ-30 questionnaire, with a mean reduction of six to 12 points compared to the general population in five of the six EORTC function subscales: global health, physical functioning, role functioning, cognitive functioning, and social functioning. A change of five or more points on this scale is considered a clinically meaningful difference. (3,4)

Patients with PNH also reported a substantially more severe level of fatigue as measured by the FACIT-Fatigue scale, with a 7.3 point reduction compared to the general population. A change of three or more points on this scale is considered a clinically meaningful difference. (5)

In the six months before enrolling in the study, one in four patients (26%) were hospitalized, and one in three patients with a paid job (33%) missed work due to PNH. At least one in six patients (16%) reported not working or worked less due to PNH. Patients with a history of thrombosis had an increased risk of hospitalization, being unemployed, or working less. Patients who reported abdominal pain, dyspnea, or icterus had an increased risk of hospitalization, missed work, or being unemployed (all p<.05).

"Just a decade ago, we knew very little about PNH. Today, with the growing PNH Registry, we're amassing valuable data that help us better understand and manage patients with this disease," said Petra Muus, M.D., Ph.D., PNH Registry investigator and associate professor of hematology at the Radboud University Nijmegen Medical Center, Nijmegen, Netherlands. "We now have a more complete and quantitative picture of the debilitating nature of PNH and how it affects patients' abilities to lead healthy, productive lives."

The PNH Registry: Blood Transfusions in PNH Patients with and without Aplastic Anemia

A second set of PNH Registry data were presented in a poster session yesterday titled, "Use of Blood Transfusion in Paroxysmal Nocturnal Hemoglobinuria Patients with and without Aplastic Anemia in the Global PNH Registry." (6) The study aimed to characterize the use of transfusions among PNH patients with and without underlying history of aplastic anemia (AA), a type of BMD.

The registry data indicate that patients with AA have a similar likelihood of elevated hemolysis — which drives the life-threatening complications of PNH — as do patients without BMD. At enrollment, 31.8% of PNH patients had a history of AA, while 49.2% had no history of BMD.

For patients with clone sizes <10%, 10-49%, and >50%, LDH multiples of upper limit of normal for AA and no BMD patients were 0.90 and 1.01, 1.55 and 2.00, and 4.70 and 4.96, respectively.

In addition, as compared to PNH patients without AA, patients with PNH and a history of AA reported similar frequency of abdominal pain and fatigue, more bruising and bleeding, and less dysphagia and hemoglobinuria. The analysis showed that approximately 40% of patients did not require a transfusion in the year prior to enrollment, regardless of AA history.

"These data add to the growing body of knowledge we're gaining through the PNH Registry, which already has made significant strides in helping us define PNH treatment objectives and best practices," said Hubert Schrezenmeier, M.D., Institute of Transfusion Medicine and Immunogenetics, Red Cross Blood Transfusion Services, Baden-Württemberg-Hessen, Ulm, Germany. "By joining the Registry, patients and physicians can help create a more robust set of data to improve the diagnosis and treatment of this rare, life-threatening disease."

The PNH Registry is designed to increase medical understanding of PNH and facilitate diagnosis of the disease. The PNH Registry collects data from patients with PNH irrespective of clone size or treatment status. As of October 31, 2010, the PNH Registry has enrolled 740 patients from 141 clinical sites in 19 countries, and is currently open to enrollment. Contact pnhregistry@iconplc.com or visit www.pnhsource.com to learn more about PNH and the PNH Registry.

About PNH

PNH is an ultra-rare blood disorder in which chronic uncontrolled activation of complement, a component of the normal immune system, results in hemolysis (destruction of the patient's red blood cells). PNH strikes people of all ages, with an average age of onset in the early 30s. (7) Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger. (8) PNH develops without warning and can occur in men and women of all races, backgrounds and ages. PNH often goes unrecognized, with delays in diagnosis ranging from one to more than 10 years. (9) It is estimated that approximately one-third of patients with PNH do not survive more than five years from the time of diagnosis. (9) PNH has been identified more commonly among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndromes (MDS). (10,11,12) In patients with thrombosis of unknown origin, PNH may be an underlying cause. (7) More information on PNH is available at www.pnhsource.com.

About Soliris

Soliris is a first-in-class terminal complement inhibitor developed from the laboratory through regulatory approval and commercialization by Alexion. Soliris has been approved in the U.S., European Union, Japan and other territories as the first treatment for patients with PNH, an ultra-rare, debilitating and life-threatening blood disorder defined by chronic uncontrolled complement activation which causes chronic hemolysis, or the destruction of red blood cells. Prior to these approvals, there were no therapies specifically available for the treatment of patients with PNH. Eculizumab (Soliris) is not approved for the treatment of aHUS, transplant or other indications other than PNH. Alexion's innovative approach to complement inhibition has received some of the pharmaceutical industry's highest honors: the 2008 Prix Galien USA Award for Best Biotechnology Product with broad implications for future biomedical research and the 2009 Prix Galien France Award in the category of Drugs for Rare Diseases. More information on Soliris is available at www.soliris.net.

Important Safety Information

Soliris is generally well tolerated in patients with PNH. The most frequent adverse events observed in clinical studies of patients with PNH were headache, nasopharyngitis (runny nose), back pain and nausea. Treatment with Soliris should not alter

anticoagulant management because the effect of withdrawal of anticoagulant therapy during Soliris treatment has not been established.

The U.S. product label for Soliris also includes a boxed warning: "Soliris increases the risk of meningococcal infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Vaccinate patients with a meningococcal vaccine at least two weeks prior to receiving the first dose of Soliris; revaccinate according to current medical guidelines for vaccine use. Monitor patients for early signs of meningococcal infections, evaluate immediately if infection is suspected, and treat with antibiotics if necessary." During PNH clinical studies, two out of 196 vaccinated PNH patients treated with Soliris experienced a serious meningococcal infection. Prior to beginning Soliris therapy, all patients and their prescribing physicians are encouraged to enroll in the PNH Registry, which is part of a special risk-management program that involves initial and continuing education and long-term monitoring for detection of new safety findings.

About Alexion

Alexion Pharmaceuticals, Inc. is a biopharmaceutical company working to develop and deliver life-changing drug therapies for patients with serious and life-threatening medical conditions. Alexion is engaged in the discovery, development and commercialization of therapeutic products aimed at treating patients with a wide array of severe disease states, including hematologic and kidney diseases, transplant, other inflammatory disorders, and cancer. Soliris is Alexion's first marketed product. Alexion is evaluating other potential indications for Soliris as well as other formulations of eculizumab for additional clinical indications, and is pursuing development of other antibody product candidates in early stages of development. This press release and further information about Alexion Pharmaceuticals, Inc. can be found at: www.alexionpharma.com.

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Safe Harbor Statement

This news release contains forward-looking statements, including statements related to potential health and medical benefits of Soliris (eculizumab) for the treatment of patients with PNH. Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ from those expected, including for example, decisions of regulatory authorities regarding marketing approval or material limitations on the marketing of Soliris for its current or potential new indications, the possibility that results of published reports or clinical trials are not predictive of safety and efficacy results of Soliris in broader patient populations, the possibility that initial results of commercialization are not predictive of future rates of adoption of Soliris, the risk that third parties won't agree to license any necessary intellectual property to Alexion on reasonable terms or at all, the risk that third party payors will not reimburse for the use of Soliris at acceptable rates or at all, and a variety of other 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 Quarterly Report on Form 10-Q for the period ended September 30, 2010, and in Alexion's other filings with the Securities and Exchange Commission. Alexion does not intend to update any of these forward-looking statements to reflect events or circumstances after the date hereof, except when a duty arises under law.

References

(1) Abstract 4241 entitled "Association Between Elevated Hemolysis at Diagnosis and Early Mortality and Risk of Thrombosis in Paroxysmal Nocturnal Hemoglobinuria (PNH) Patients with Cytopenia," presented in a poster session at the 52nd American Society of Hematology (ASH) Annual Meeting and Exposition, December 6, 2010, at 6:00 p.m. by Dr. Jin Seok Kim.

(2) Abstract 1525 entitled "Evaluation of Paroxysmal Nocturnal Hemoglobinuria Disease Burden: The Patient's Perspective. A Report from the International PNH Registry," presented in a poster session December 4, 2010, at 5:30 p.m. by Dr. Petra Muus.

(3) Osoba et al J Clin Oncol 1998; 16:139-144.

(4) EORTC QLQ-C30 Reference Values, 2008.

(5) Cella et al. Cancer 2002; 94:528-538

(6) Abstract 2241 entitled "Use of Blood Transfusions in Paroxysmal Nocturnal Hemoglobinuria Patients with and without Aplastic Anemia Enrolled in the Global PNH Registry," presented in a poster session December 5, 2010, at 6:00 p.m. by Dr. Hubert Schrezenmeier.

(7) Socié G, Mary J Yves, de Gramont A, et al. Paroxysmal nocturnal haemoglobinuria: long-term follow-up and prognostic factors. Lancet. 1996: 348:573-577.

(8) Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood. 2005;106 (12):3699-3709.

(9) Hillmen P, Lewis SM, Bessler M, Luzzatto L, Dacie JV. Natural history of paroxysmal nocturnal hemoglobinuria. N Engl J Med. 1995; 333:1253-1258.

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(11) Iwanga M, Furukawa K, Amenomori T, et al. Paroxysmal nocturnal haemoglobinuria clones in patients with myelodysplastic syndromes. Br J Haematol. 1998;102 (2):465-474.

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