



Soliris(R) Improved Fatigue Independent of Changes in Anemia in Patients with PNH by Controlling Hemolysis

Data Suggest Role of Hemolysis in PNH-Related Fatigue Presentation at the European Hematology Association 13th Congress

CHESHIRE, Conn., June 15, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- Soliris(R) (eculizumab) therapy improved the often disabling fatigue experienced by patients with the rare blood disorder paroxysmal nocturnal hemoglobinuria (PNH) independent of improvements in anemia, according to data presented today at the European Hematology Association (EHA) 13th Congress in Copenhagen (abstract number 0903). These data suggest that fatigue experienced by patients with PNH is related directly to hemolysis -- the red blood cell destruction that defines the disease -- and can be improved independent of correction of anemia.

In clinical trials with Soliris, PNH patients experienced a substantial improvement in PNH-related fatigue independent of changes in their anemia. This improvement was larger than the improvement in fatigue reported in a separate study of anemic cancer patients treated with erythropoietin (EPO). Furthermore, in contrast to the improvement in fatigue of anemic cancer patients treated with EPO which occurred only when anemia was also improved, Soliris-treated PNH patients experienced improvements in fatigue independent of changes in their anemia. Taken together, these data suggest that hemolysis likely contributes to fatigue experienced by patients with PNH independent of the contribution of hemolysis to anemia in these patients.

The data were highlighted in an oral presentation to the EHA Congress by Anita Hill, MB, ChB, Consultant Hematologist at Bradford Teaching Hospitals, UK, lead author of the abstract titled, "Improvement in Fatigue with Eculizumab Treatment of Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Occurs Independent of Changes in Anemia." (1)

"Complement-mediated hemolysis is the defining characteristic of PNH and the cause of the serious clinical consequences of the disease, which include disabling fatigue," said Dr. Hill. "The data presented at EHA help us to understand that fatigue in PNH is tied much more closely to hemolysis than to anemia, and emphasize the importance of eculizumab therapy in providing a better quality of life to patients with PNH, independent of any changes in anemia they experience."

Soliris, developed by Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) was approved in the U.S. and European Union in 2007; Soliris is indicated in the U.S. for the treatment of patients with PNH to reduce hemolysis and is indicated in the EU for the treatment of patients with PNH. PNH is a rare, debilitating and life-threatening blood disease in which hemolysis, caused by the patient's own immune system, can cause thromboses (blood clots), disabling fatigue, anemia, impaired quality of life, shortness of breath, recurrent pain, kidney disease and intermittent episodes of dark-colored urine (hemoglobinuria). (2-4)

Soliris, Hemolysis and Fatigue in PNH

Fatigue levels in patients with PNH are often severe and similar to those experienced by anemic cancer patients. Soliris has been shown to reduce substantially the frequently disabling fatigue associated with PNH. The data presented today provide additional insight into the mechanism through which Soliris positively impacts PNH-related fatigue. While treatments designed to improve anemia can improve fatigue in both PNH and cancer, these data demonstrate that fatigue in PNH is also related directly to chronic hemolysis and can be improved independent of correction of anemia. Soliris has also been associated with other significant benefits in patients with PNH, including reduction in hemolysis and reduction in thrombotic events during treatment phase compared to the same period of time prior to treatment. (5-7)

In the presentation by Dr. Hill, data on 164 patients with PNH were derived from two Phase 3 studies of Soliris as a treatment for PNH: TRIUMPH, a six-month, double-blind, placebo-controlled study, and SHEPHERD, a 12-month, open-label study. Data on anemic cancer patients were obtained from a published report.(8) Patient-reported fatigue in both groups of patients was determined utilizing the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale. Anemia was measured by levels of hemoglobin, and hemolysis was measured by levels of lactate dehydrogenase (LDH). Key findings included the following:

- * While intravascular hemolysis reduction (decreased LDH) and anemia improvement (increased hemoglobin) were both significantly associated with fatigue improvement (odds ratio 1.11, $P < 0.001$ and 1.29, $P = 0.005$, respectively), hemolysis reduction was predictive of an improvement in fatigue independent of an improvement in anemia in patients with PNH

(1.07, P=0.028).

- * The improvement in fatigue was greater (P=0.002) in Soliris-treated PNH patients compared to EPO-treated anemic cancer patients.
- * When the magnitude of clinical impact was analyzed by using standard descriptors for the Effect Size (ES) measurement of fatigue in both groups, (9)
 - * PNH patients treated with Soliris experienced a large improvement in fatigue, (ES: +1.0) when the hemoglobin level increased as compared to anemic cancer patients treated with EPO who experienced only a small improvement in fatigue (ES: +0.48).
 - * Similarly, PNH patients treated with Soliris experienced a moderate improvement in fatigue (ES:+0.72) when hemoglobin levels did not improve compared to EPO-treated anemic cancer patients for whom fatigue scores did not change meaningfully (ES:+0.15) when hemoglobin levels did not improve.
 - * Importantly, Soliris-treated PNH patients still experienced a moderate improvement in fatigue (ES: +0.61) even when hemoglobin levels decreased, while EPO-treated anemic cancer patients experienced a small worsening of fatigue (ES:-0.33) when hemoglobin levels decreased.

The improvement in fatigue associated with Soliris therapy in clinical trials was observed within the first week of treatment and has been sustained for more than two years. (10)

"As in cancer patients, fatigue in PNH patients is often severe enough to make the ordinary activities of daily life impossible," said Leonard Bell, M.D., Chief Executive Officer of Alexion. "This study indicates that patients can experience life-changing improvements in fatigue with long-term Soliris therapy regardless of changes in their anemia. This, and the other compelling clinical benefits that Soliris offers patients with PNH, are the basis for our commitment that every patient who can benefit from Soliris should have access to it."

About PNH

PNH is a rare blood disease that affects an estimated 8,000 to 10,000 people in North America and Europe and, using similar prevalence estimates, potentially 1,000 to 2,000 patients in Japan. (11) Although affecting all age groups, PNH often has an average age of onset in the early 30's. (12) Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger. (4) 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 often ranging from one to more than 10 years. (3) The estimated median survival for PNH patients is between 10 and 15 years from the time of diagnosis. (3,12)

PNH has been identified more commonly among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndrome (MDS). (13,14,15,16) In patients with thrombosis of unknown origin, PNH may be an underlying cause. (3,12)

Prior to approval of Soliris, there were no therapies specifically available for the treatment of PNH. PNH treatment was limited to symptom management through periodic blood transfusions, non-specific immunosuppressive therapy and, infrequently, bone marrow transplantations -- a procedure that carries considerable mortality risk. (4,17)

About Soliris

Soliris was approved in March 2007 by the U.S. Food and Drug Administration (FDA) as the first treatment for PNH, a rare, debilitating and life-threatening blood disorder defined by hemolysis, or the destruction of red blood cells. In June 2007, the European Commission (EC) also approved the use of Soliris for the treatment of patients with PNH. Soliris is the first therapy approved in Europe for the treatment of PNH and was the first medicinal product to receive EC approval under the EMEA Accelerated Assessment Procedure.

Important Safety Information

Soliris is generally well tolerated. The most frequent adverse events observed in clinical studies were headache, nasopharyngitis (a 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. 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 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 enrolled in the Soliris Safety 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.

Please see full prescribing information at www.soliris.net.

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 diseases, cancer, and autoimmune disorders. In March 2007, the FDA granted marketing approval for Alexion's first product, Soliris, for all patients with PNH, and Alexion began commercial sale of Soliris in the U.S. during April 2007. In June 2007, the EC granted marketing approval for Soliris in the European Union for all patients with PNH. 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.alexionpharm.com.

Safe Harbor Statement

This news release contains forward-looking statements, including statements related to potential health and medical benefits from Soliris. 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, delays in arranging satisfactory manufacturing capability and establishing commercial infrastructure, delays in developing or adverse changes in commercial relationships, the possibility that results of 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, the risk that estimates regarding the number of PNH patients are inaccurate, the risk that pending litigation may be resolved adversely, 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 March 31, 2008 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.

(1) Hill A, Muus P, Socie G, et al. Improvement in fatigue with eculizumab treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) occurs independent of changes in anemia. [abstract #1309]. Presented at 13th Congress of the European Hematology Association Annual Meeting; June 15, 2008; Copenhagen, Denmark.

(2) Rother RP, Bell L, Hillmen P, Gladwin M. The clinical sequelae of intravascular hemolysis and extracellular plasma hemoglobin: a novel mechanism of human disease. *JAMA*. 2005;293:1653-1662.

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

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

(5) Hillmen P, Muus P, Duhrsen U et al. Effect of the complement inhibitor eculizumab on thromboembolism in patients with paroxysmal nocturnal hemoglobinuria. *Blood*. 2007; 100:4123-4128.

(6) Hillmen P, Young NS, Schubert J et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. *N Engl J Med*. 2006;355:1233-1243.

(7) Brodsky RA, Young NS, Antonioli E et al. Multicenter phase 3 study of the complement inhibitor eculizumab for the treatment of patients with paroxysmal nocturnal hemoglobinuria. *Blood*. 2008;111:1840-1847.

- (8) Cella D, Eton DT, Lai JS, Peterman AH, Merkel DE. Combining anchor and distribution-based methods to derive minimal clinically important differences on the Functional Assessment of Cancer Therapy (FACT) anemia and fatigue scales. *J Pain Symptom Manage*. 2002;24(6):547-61.
- (9) Cella D, Kallich J, McDermott A, Xu X. The longitudinal relationship of hemoglobin, fatigue and quality of life in anemic cancer patients: results from five randomized clinical trials. *Ann Oncol*. 2004;15:979-86.
- (10) Socie G, Hillmen P, Muus P et al. Sustained improvements in transfusion requirements, fatigue and thrombosis with eculizumab treatment in paroxysmal nocturnal hemoglobinuria [abstract]. *Blood*. 2007;110 (11):1072a.
- (11) Hill A, Platts PJ, Smith A et al. The incidence and prevalence of paroxysmal nocturnal hemoglobinuria (PNH) and survival of patients in Yorkshire [abstract]. *Blood*. 2006;108(11):985.
- (12) Socie G, Mary J Yves, de Gramont A, et al. Paroxysmal nocturnal haemoglobinuria: long-term follow-up and prognostic factors. *Lancet*. 1996; 348:573-577.
- (13) Johnson RJ, Hillmen P. Paroxysmal nocturnal hemoglobinemia: Nature's gene therapy? *J Clin Path: Mol Pathol*. 2002;55:145-152.
- (14) Wang H, Chuhjo T, Yasue S, Omine M, Naka S. Clinical significance of a minor population of paroxysmal nocturnal hemoglobinuria-type cells in bone marrow failure syndrome. *Blood*. 2002;100 (12):3897-3902.
- (15) 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.
- (16) Maciejewski JP, Rivera C, Kook H, Dunn D, Young NS. Relationship between bone marrow failure syndromes and the presence of glycosphosphatidyl inositol-anchored protein-deficient clones. *Br J Haematol*. 2001;115 (4):1015- 1022.
- (17) Hill A, Richards S, Hillmen P. Recent developments in the understanding and management of paroxysmal nocturnal haemoglobinuria. *Br J Haematol*. 2007;137 (3):181-192.

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