



## Soliris(R) Reduced Hemolysis, Lowered Thrombosis Rate and Improved Quality of Life in Patients with PNH Who Had Previously Never Been Transfused

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CHESHIRE, Conn., Dec 07, 2009 (BUSINESS WIRE) -- New data presented today demonstrate the severe clinical burden of [paroxysmal nocturnal hemoglobinuria \(PNH\)](#) and the clinical benefits of [Soliris\(R\) \(eculizumab\)](#) in 44 patients with no history of prior blood transfusions. Prior to Soliris treatment, these never-transfused patients with PNH demonstrated increased intravascular hemolysis (red blood cell destruction), 87% reported impaired quality of life, and 28% had a history of clinically evident thrombosis (blood clots).

Soliris, a first-in-class terminal complement inhibitor developed by [Alexion Pharmaceuticals, Inc.](#) (Nasdaq: ALXN), significantly reduced hemolysis in all patients assessed in this retrospective study. 91% of patients with quality of life assessments both before and during Soliris treatment showed improvement in their quality of life during Soliris treatment. Researchers also observed a significant reduction in clinically evident thrombosis, from 7.85 events per 100 patient years to zero events ( $p < 0.001$ ) following Soliris treatment.

The data were presented today at the [51st Annual Meeting of the American Society of Hematology \(ASH\)](#) in a poster titled, "[Clinical Impact of Unregulated Terminal Complement Activity in Never-Transfused Patients with Paroxysmal Nocturnal Hemoglobinuria.](#)"

"These data show that patients with PNH may have significant clinical consequences from their disease, even if they did not have transfusion requirements and even if hemoglobin levels were not significantly decreased. In this study, nearly all patients with PNH and no prior history of transfusions experienced intravascular hemolysis, which can result in debilitating fatigue and impaired quality of life and serious and life-threatening complications such as thrombosis, kidney damage, and pulmonary hypertension," said Petra Muus, M.D., Ph.D. of Radboud University, Nijmegen, Netherlands. "Soliris therapy inhibited hemolysis in these patients, leading to immediate clinical benefit and potentially reducing the long-term morbidity and mortality associated with this ultra-rare disease."

"This study shows both the central role of unregulated complement activity and chronic hemolysis in PNH, and the significant clinical benefits of Soliris in all patients with PNH, regardless of pre-treatment transfusion status or hemoglobin levels," said Leonard Bell, M.D., Ph.D. Chief Executive Officer of Alexion.

### Clinical Data

In this retrospective study, researchers identified and evaluated 44 patients with PNH who had not received prior red blood cell transfusions and were considered candidates for Soliris therapy based on the physician's clinical assessment. This group of patients from France, Italy, the Netherlands, Australia and the United States ranged in age from 16 to 84 years (median 41 years) and in duration of diagnosis from 1 month to 30 years (average 3.8 years). (1)

Prior to Soliris therapy, these never-transfused patients ( $n=44$ ) overall demonstrated increased intravascular hemolysis, as measured by elevated LDH (median 1,360 U/L). Quality of life was assessed by a healthcare provider and assessments included good (no impairment), or impairment which was further characterized with any of the following terms: mild impairment, disabling or moderate fatigue, disabling abdominal pain, shortness of breath with exertion, or poor quality of life. In this analysis, 87% of patients never transfused (34/39) had impaired quality of life at baseline. Baseline levels of LDH (median 1,360 U/L), hemoglobin (median 9.9 g/dL) and Type 3 white blood cell clone size (median 70%) were not predictive of an association with impaired quality of life, nor of history of thrombosis. In the study 52% of patients with PNH and impaired quality of life had mild anemia (hemoglobin levels greater-than or equal to 10.0g/dL) and 25% had a white blood cell clone size  $< 50\%$ . Clinically evident thrombosis was relatively common, present in 28% of patients overall. Baseline hemoglobin and clone size did not predict risk of TE. The median hemoglobin level in those never transfused patients with a history of thrombosis was 10.7 g/dL, with levels ranging from severe anemia (8.0 g/dL) to normal levels (14.9 g/dL). Thrombosis was observed in 33% of patients with PNH white blood cell clone size  $< 50\%$  ( $n=8$ ) and in 30% of patients with PNH white blood cell clone size  $> 50\%$  ( $n=24$ ).

Patients received 600 mg of Soliris every 7 days (+/- 2 days) for 4 doses; followed by 900 mg one week later; then 900 mg every 14 days (+/- 2 days) for a median duration of 1.2 years. All patients who received Soliris ( $n=27$ ) experienced a reduction in hemolysis following treatment, as measured by a median reduction in LDH from 1,603 U/L before treatment to 380 U/L after treatment ( $p < 0.0001$ ). Among 11 patients who received a quality of life assessment both before and after treatment, 91% reported an impaired quality of prior to treatment, compared with none following Soliris therapy. Further, there was no reported thrombosis during treatment with eculizumab (11 patients with history of thrombosis) and the thrombosis event rate was significantly reduced from 7.85 to 0 (events/100-patient years;  $p < 0.001$ ).

### About PNH

PNH is an ultra-rare blood disorder that strikes people of all ages, with an average age of onset in the early 30s. (2) Patients with PNH suffer from hemolysis (red blood cell destruction) which leads to thromboses (blood clots), disabling fatigue, anemia, impaired quality of life, pulmonary hypertension, shortness of breath, recurrent pain, kidney disease and intermittent episodes of dark-colored urine (hemoglobinuria). (3,4) Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger. (3) 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. (5) It is estimated that approximately one-third of patients with PNH do not survive more than five years from the time of diagnosis. (5) Studies have shown that kidney disease accounts for 18 percent of deaths among Japanese patients with PNH. (6) PNH has been identified more commonly among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndromes (MDS). (7,8,9) In patients with thrombosis of unknown origin, PNH may be an underlying cause. (3) More information on PNH is available at [www.pnhsource.com](#).

## About Soliris

Soliris has been approved by the U.S. Food and Drug Administration (March 2007), the European Commission (June 2007), Health Canada (January 2009) and Australia's Therapeutic Goods Administration (February 2009) as the first treatment for all patients with PNH, an ultra-rare, debilitating and life-threatening blood disorder defined by chronic hemolysis, or the destruction of red blood cells. Prior to these approvals, there were no therapies specifically available for the treatment of PNH. More information on Soliris is available at [www.soliris.net](http://www.soliris.net).

## 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. 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 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, cancer, and autoimmune disorders. 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](http://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 from Soliris (eculizumab). 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 published reports or clinical trials are not predictive of safety and efficacy results of Soliris in broader patient populations, the risk that clinical trials may not be completed successfully, 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, 2009, 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. Muus P, et al. Clinical Impact of Unregulated Terminal Complement Activity in Never-Transfused Patients with Paroxysmal Nocturnal Hemoglobinuria. Presented at the 51st Annual Meeting of the American Society of Hematology, New Orleans, LA December 7, 2009; Poster Board # III-965 [Blood 2009; 114:4029]
2. 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.
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