



## **Long-Term Efficacy, Safety and Survival Outcomes of PNH Patients Treated with Soliris® (eculizumab) Reported at ASH Annual Meeting**

CHESHIRE, Conn.--(BUSINESS WIRE)-- Independent investigators reported today that patients with paroxysmal nocturnal hemoglobinuria (PNH) who were treated long-term with Soliris® (eculizumab) achieved survival comparable to that of an age- and gender-matched normal population. (1) Findings from this investigator-led analysis were reported in an oral presentation today at the 52<sup>nd</sup> American Society of Hematology (ASH) Annual Meeting and Exposition in Orlando. Soliris is a first-in-class terminal complement inhibitor developed by Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN).

PNH is an ultra-rare, life-threatening blood disorder in which uncontrolled activation of the complement system causes the chronic destruction of red blood cells (hemolysis). Historically, up to 35% of patients with PNH die within five years of diagnosis due to serious clinical outcomes including thromboembolism (TE) and chronic kidney disease (CKD). (2-7)

### **Investigator-Led Analysis Showed Sustained Efficacy and Improved Survival with Soliris**

In the analysis presented today titled, "Long Term Treatment with Eculizumab In Paroxysmal Nocturnal Hemoglobinuria (PNH): Sustained Efficacy and Improved Survival," researchers from St. James's University Hospital in Leeds, UK, compared data from 79 patients with PNH treated with Soliris for up to eight years (mean 39 months) with an age- and gender-matched normal population based on data from the UK Office of National Statistics. (1) Nearly half of the PNH patients in this analysis participated in the Soliris PNH clinical trials.

The analysis reported in the published abstract demonstrated comparable survival between patients with PNH treated with Soliris and the normal population. There were fewer thrombotic events among patients with PNH following Soliris therapy, with 34 thrombotic episodes occurring in 21 patients prior to treatment, and only two thromboses occurring in those same patients after the start of Soliris treatment. Of 64 patients treated with Soliris for at least one year, 66% became transfusion-independent for more than 12 months, and the remaining 34% showed a significant 41% reduction in the mean units transfused ( $p=0.028$ ). Investigators reported that Soliris was well tolerated.

"In these patients, we observed far fewer thromboses than expected during long-term treatment with Soliris compared with the thromboses seen pre-treatment. This is important because thromboses are common and deadly complications of PNH," noted Peter Hillmen, M.D., Ph.D., consultant hematologist at the Leeds Teaching Hospitals NHS Trust and lead study investigator. "The comparable survival rates observed between patients with PNH treated with Soliris in this analysis and the general population in the UK is very important for patients with a disease in which life expectancy is reduced substantially. This finding underlines the key role of uncontrolled complement activity in the most important adverse consequences of PNH and that protecting PNH cells from this uncontrolled attack is critical to the effective targeted therapy of the disease."

### **Clinical Study Demonstrates Long-Term Safety and Efficacy of Soliris**

In a poster presentation today titled, "Long Term Safety and Efficacy of Sustained Eculizumab Treatment in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)," researchers reported clinical findings from a multi-center study that included all 195 patients from the pilot and Phase 3 clinical trials of Soliris, as well as from subsequent extension studies. (8) Patients were treated with Soliris for up to 5.5 years (median 29 months). Efficacy findings were reported for patients at 36 months of Soliris treatment.

Within one week, hemolysis, as assessed by levels of LDH, was reduced in 100% of patients treated with Soliris and was sustained throughout the treatment period ( $p<0.000001$ ). Overall survival was 97.6% (95% CI 93.7-99.1) at 36 months. In addition, TE events were reduced by 81%, from 52 pre-treatment events to 10 events during Soliris therapy using matched time analysis ( $P<0.0005$ ). The prevalence of CKD was reduced from 69% of patients at baseline to 31% ( $n=29$ ) after 36 months of treatment, consistent with previously published results. (4)

Soliris was well-tolerated during the treatment period. The most common adverse events reported included headache (55%), nasopharyngitis (50%), upper respiratory tract infection (41%), diarrhea (35%), and nausea (32%). There were two cases of meningococcal sepsis, which were both successfully treated without sequelae.

"These long-term data show that the compelling clinical benefits and safety profile of Soliris seen in shorter-term studies were sustained over 36 months," said lead investigator Robert A. Brodsky, M.D., director of the Division of Hematology and professor of medicine and oncology at Johns Hopkins Medicine in Baltimore. "Soliris is the first and only medication approved for the

treatment of patients with PNH, and we now have evidence that this therapy can provide long-term reduction in hemolysis with documented safety for patients with this life-threatening condition."

## **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. (9) Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger. (10) 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. (11) It is estimated that approximately one-third of patients with PNH do not survive more than five years from the time of diagnosis. (11) PNH has been identified more commonly among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndromes (MDS). (12-14) In patients with thrombosis of unknown origin, PNH may be an underlying cause. (9) More information on PNH is available at [www.pnhsource.com](http://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. 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](http://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](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 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 639 entitled "Long Term Treatment with Eculizumab in Paroxysmal Nocturnal Hemoglobinuria (PNH): Sustained Efficacy and Improved Survival," presented in an oral session at the 52<sup>nd</sup> American Society of Hematology (ASH) Annual Meeting and Exposition, December 6, 2010, at 3:15 p.m. by Dr. Richard Kelly.
- (2) Hillmen P et al. *Am. J. Hematol.* 2010; 85:553—559.
- (3) Rother RP, et al. *JAMA.* 2005;293:1653-1662.
- (4) Hillmen P, et al. *N Engl J Med.* 2004;350:552-559.
- (5) Hillmen P, et al. *N Engl J Med.* 2006;355:1233-1243.
- (6) Brodsky RA, et al. *Blood.* 2008;111:1840-7
- (7) Hillmen P, et al. *Blood.* 2007;100:4123-4128.
- (8) Abstract 4237 entitled "Long Term Safety and Efficacy of Sustained Eculizumab Treatment in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)," presented in a poster session at the 52<sup>nd</sup> American Society of Hematology (ASH) Annual Meeting and Exposition, December 6, 2010, at 6:00 p.m. by Dr. Robert A. Brodsky.
- (9) 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.
- (10) Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. *Blood.* 2005;106 (12):3699-3709.
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