



Phase 2 Study of Eculizumab (Soliris®) in Patients with aHUS Resistant to Plasma Therapy Met Primary and Secondary Endpoints with High Statistical and Clinical Significance

Eculizumab Reduced Thrombotic Microangiopathy, Restored Kidney Function and Improved Quality of Life as Reported at ASN Meeting

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) announced today that a Phase 2 clinical study investigating Soliris® (eculizumab) as a treatment for patients with atypical Hemolytic Uremic Syndrome (aHUS) who are resistant to plasma therapy met primary and key secondary endpoints with high levels of statistical and clinical significance, according to results presented today at the American Society of Nephrology (ASN) annual meeting in Denver. The new data are consistent with an earlier interim analysis contained in the abstract of today's presentation and published online by ASN on October 20, 2010. Soliris is a first-in-class terminal complement inhibitor discovered and developed by Alexion.

aHUS is an ultra-rare, chronic and life-threatening disease in which uncontrolled complement activation causes blood clots in small blood vessels throughout the body (thrombotic microangiopathy, or TMA) leading to kidney failure, stroke, heart attack and death.^{1,2,3} Because aHUS is a genetic disease, patients have a life-long risk of sudden and severe complications of uncontrolled complement activation. Approximately 60% of patients with aHUS require dialysis, undergo a kidney transplant, or die within one year of diagnosis.⁴

Patients Resistant to Plasma Therapy

In an oral presentation today, researchers reported final data from a Phase 2 study of eculizumab in patients with aHUS who were resistant or intolerant to plasma therapy.⁵ This analysis included 17 adolescent and adult patients who received eculizumab therapy for 26 weeks. The prospective primary endpoint was the change in platelet count from baseline, a measure of TMA, at 26 weeks. Key prospective secondary endpoints included TMA event-free status (defined as at least 12 consecutive weeks of stable or increasing platelet counts, absence of plasma therapy, and no new dialysis), improvements in chronic kidney disease (CKD) stage, and change in quality of life.

Improvement in Platelet Count: A Measure of TMA Reduction

The primary endpoint of the study, change in platelet count, increased significantly through 26 weeks of treatment compared to baseline ($p < 0.0001$) and was increased $96 \pm 21 \times 10^9/L$ at 26 weeks of treatment with eculizumab. Researchers reported that following the first infusion of eculizumab, platelet count increased significantly at Day 7 ($p = 0.02$). A key secondary endpoint, TMA event-free status, was achieved in 88% of patients (15 of 17; 95% CI 64-100).

Improvement in Kidney Function

Researchers reported significant improvement in kidney function with sustained eculizumab therapy over the 26-week dosing period. Estimated glomerular filtration rate (eGFR), a standard measure of kidney function, increased sufficiently to result in an improvement of at least one stage in CKD in 65% of patients (11 of 17, 95% CI 33-82), and eGFR increased less than one CKD stage in four additional patients. Of the seven patients who received dialysis before entering the study, five became dialysis-free following treatment with eculizumab and remained so for the entire 26 weeks.

Improvement in Quality of Life Measures

Quality of life as measured by the summary index of the EuroQol 5D improved significantly through 26 weeks. The improvement was highly statistically significant compared to baseline ($p < 0.0001$) and was improved 0.33 ± 0.09 at 26 weeks which was more than five times the level generally considered to be a clinically meaningful change.⁶

All reported study results were similar for patients with and without complement regulatory protein mutations or auto-antibodies. Eculizumab was well tolerated in the study, and all patients remain alive. There were no cases of meningococcal infection in the trial. The most frequent adverse events were anemia, headache, diarrhea and vomiting. Two patients withdrew from the study; one patient was withdrawn after it was subsequently determined that the patient met an exclusion criterion and one patient withdrew from the study due to an adverse event deemed unrelated to eculizumab.

"These ground-breaking results show that eculizumab significantly increased platelets and reduced the life-threatening blood

clot process that caused severe damage to the kidney and other organs in these patients with aHUS," said Christophe Legendre, M.D., a study investigator and professor of nephrology at University Rene Descartes-Hôpital Necker in Paris. "The stabilization and improvement of kidney function observed in this study is particularly meaningful because these patients are resistant to plasma therapy, one of the current management strategies for aHUS."

Patients on Plasma Therapy Chronically

In a poster session yesterday, researchers presented interim results from a separate Phase 2 study of 20 adult and adolescent patients with aHUS who were receiving plasma therapy chronically prior to starting treatment with eculizumab.⁷ These interim results were the same as previously reported. The prospective primary endpoint in this study was TMA event-free status, which was achieved by a significant 87% of patients in the interim 12-week analysis of 15 patients (13 of 15; 95% CI 60-98). The analysis also met a key prospective secondary endpoint: none of the patients treated with eculizumab required TMA intervention.

"aHUS is a devastating disease and patients are chronically at risk for disease progression including sudden onset of stroke, heart attack, kidney failure and death, even if they are treated frequently with currently available interventions," said Petra Muus, M.D., Ph.D., study investigator and associate professor of hematology at Radboud University Medical Center in the Netherlands. "These findings show that studied patients demonstrated an immediate response and sustained efficacy with eculizumab, giving the aHUS community hope for reducing the need for new dialysis and plasma therapy."

Eculizumab appeared to be well tolerated in the study. The most frequent adverse events were diarrhea, nausea, headache and hypertension (all mild to moderate).

"The results from these Phase 2 studies suggest that it may be possible to change the course of aHUS by targeting chronic uncontrolled complement activation," said Leonard Bell, M.D., Chief Executive Officer of Alexion. "The significant increase in platelet count, reduction in TMA, restored kidney function, and improved quality of life reported today indicates that eculizumab may have the potential to transform the lives of patients with this devastating disease and their families. We continue to advance this important program."

Pediatric Study

Alexion has commenced a Phase 2, open-label, single-arm, multi-center study of eculizumab in pediatric patients with aHUS in the United States, European Union and Canada. Information about the trial is posted to www.clinicaltrials.gov, Identifier Number NCT01193348. Physicians and families who are interested in participating in this clinical trial can learn more by contacting Alexion by e-mail at clinicaltrials@alxn.com, or by visiting the Alexion website at www.alexionpharma.com and clicking on the clinical trials link.

About aHUS

aHUS is a chronic, ultra-rare disease characterized by thrombotic microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body, causing a reduction in platelet count (thrombocytopenia) and life-threatening damage to the kidney, brain, heart and other vital organs.¹⁻³ Approximately 60 percent of patients with aHUS require dialysis or a kidney transplant or die within a year of diagnosis, despite currently available care.⁴ The majority of patients with aHUS who receive a kidney transplant experience severe complications of the disease, and more than 90 percent of these patients experience failure of the donor kidney.⁸

aHUS is a progressive disease caused by uncontrolled activation of the complement system due to genetic deficiency in complement regulatory genes. With genetic deficiency of naturally occurring complement inhibitors, patients experience life-long uncontrolled activation of the complement system, causing ongoing inflammation and blood clots in vital organs.^{9,10} In patients with aHUS, uncontrolled complement activation results in an ongoing risk of sudden and catastrophic life-threatening complications.

About Soliris

Soliris is not approved for the treatment of patients with aHUS and is being provided to patients in clinical studies on an investigational basis. Soliris has been approved by the healthcare authorities in the United States, European Union, Japan and other countries as the first treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH), a rare, debilitating and life-threatening blood disorder defined by hemolysis, or the destruction of red blood cells. Prior to these approvals, there was no therapy specifically available for the treatment of PNH. Soliris is a first-in-class terminal complement inhibitor developed from the laboratory through regulatory approval and commercialization by Alexion.

Patients with PNH in more than 20 countries now have access to Soliris therapy through national or private healthcare

providers. As the first terminal complement inhibitor to be approved in countries around the world for any indication, Soliris represents a long-sought breakthrough in medical innovation. 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 anticipated clinical development milestones and potential health and medical benefits of Soliris (eculizumab) for the potential treatment of patients with aHUS. 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 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, 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) Alexion Pharmaceuticals. Soliris in Other Kidney Disorders. Alexion Pharmaceuticals Corporate Website 2010 September 24 Available from: URL: <http://www.alexionpharma.com/RandD/Soliris%20In%20Other/kidney%20disorders.aspx#A1>
- (2) Benz K, Amann K. Thrombotic microangiopathy: new insights. *Curr Opin Nephrol Hypertens* 2010 May;19(3):242-7.
- (3) Tsai HM. The molecular biology of thrombotic microangiopathy. *Kidney Int* 2006 Jul;70(1):16-23.
- (4) Loirat C, Noris M, Fremeaux-Bacchi V. Complement and the atypical hemolytic uremic syndrome in children. *Pediatr Nephrol*. 2008;23(11):1957-1972
- (5) Abstract 1338 entitled "Safety and Efficacy of Eculizumab in aHUS Patients Resistant to Plasma Therapy: Interim Analysis

from a Phase II Trial," presented in an oral presentation at the American Society of Nephrology (ASN) Annual Meeting on Saturday, November 20, 2010 at 5:30 p.m. by Dr. Christophe Legendre.

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(7) Abstract 157 entitled "Safety and Efficacy of Eculizumab in aHUS Patients on Chronic Plasma Therapy: Interim Analysis of a Phase II Trial," presented in a poster presentation at the American Society of Nephrology (ASN) Annual Meeting on Friday, November 19, 2010 from 10:00 a.m. - 2:30 p.m. by Dr. Petra Muus.

(8) Bresin E, Daina E, Noris M, Castelletti F, Stefanov R, Hill P, et al. Outcome of renal transplantation in patients with non-Shiga toxin-associated hemolytic uremic syndrome: prognostic significance of genetic background. Clin J Am Soc Nephrol 2006 Jan;1(1):88-99.

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