



New Data from Global aHUS Registry Presented at ASN 2016 Show a Three-Fold Reduction in Post-Transplant Dialysis in Patients Initiating Soliris® (eculizumab) Treatment Prior to Transplant Compared to Initiating Treatment Post-Transplant

November 17, 2016

- Reduction in Incidence of Chronic Dialysis was also Observed in Patients Initiating Soliris Treatment Prior to Transplant -

- Reduction in Dialysis was Sustained Post-Transplant with Ongoing Treatment -

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq:ALXN) announced today that researchers presented new data from an analysis of patients enrolled in the Global atypical Hemolytic Uremic Syndrome (aHUS) Registry, demonstrating that initiation of Soliris® (eculizumab) prior to kidney transplant reduces the risk of dialysis post-transplant in patients with aHUS. Specifically, results showed that starting Soliris prior to transplant reduced the likelihood of dialysis three-fold compared to initiating Soliris post-transplant. There was also a four-fold reduction in chronic dialysis when Soliris was initiated prior to transplant and maintained in accordance with labeled dosing. Further, the need for dialysis increased after transplant if Soliris was discontinued.¹ These data were presented in an oral session at the 2016 annual meeting of the American Society of Nephrology (ASN) in Chicago.

"Patients suffering from the devastating effects of aHUS are at a high risk of graft loss following kidney transplant due to the ongoing, unpredictable risk of complement-mediated thrombotic microangiopathy," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "The data presented at ASN show that initiating Soliris prior to transplant has the potential to reduce the risk of both acute and chronic dialysis, and demonstrate the benefit of sustained treatment in patients with aHUS."

aHUS is a genetic, chronic, and progressive ultra-rare disease associated with vital organ failure and premature death.^{2,3,4} Soliris is approved in nearly 40 countries as a treatment for patients with aHUS and in nearly 50 countries as a treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH), a debilitating, ultra-rare and life-threatening blood disorder characterized by complement-mediated hemolysis (destruction of red blood cells). Both aHUS and PNH are caused by chronic uncontrolled complement activation.

Researchers at ASN will also present an update on renal survival characteristics of patients enrolled in the Global aHUS Registry in a poster presentation at ASN on Saturday, November 19 (SA-PO783).⁵

Timing of Eculizumab Treatment and the Need for Dialysis in Patients with aHUS Who Receive a Kidney Transplant (TH-OR095)¹

In an oral session, Andrew Siedlecki, M.D., Instructor in Medicine, Brigham and Women's Hospital, Boston, presented results from an analysis of patients enrolled in the Global aHUS Registry evaluating the rate of dialysis in 147 patients with aHUS who had a kidney transplant and were treated with Soliris, and had at least 1 year of follow-up post-transplant. The study compared all patients who started on Soliris therapy before or at the time of the transplant (n=69, median age 34 at current transplant, including patients receiving non-labeled dosing) to those who started on Soliris after the transplant (n=78, median age 35). A sub-analysis was also performed on the patients who continued to receive labeled dosing of Soliris initiated prior to transplant (n=53) compared to those who were initiated on and continued to receive labeled dosing of Soliris after the transplant (n=65).

Dr. Siedlecki reported that:

- Six out of 69 patients who started on Soliris therapy before transplant required dialysis, compared to 28 out of 78 who initiated Soliris treatment post-transplant. The adjusted hazard ratio was 3.0 (95% CI 1.2-7.7) comparing dialysis events in the two populations, indicating a three-fold increase in the likelihood of dialysis in the patients who initiated Soliris treatment post-transplant.
- In the sub-analysis of patients receiving labeled dosing, 4 out of 53 patients who started Soliris therapy before transplant required dialysis, compared to 23 out of 65 patients who initiated Soliris treatment post-transplant, indicating a nearly three-fold increase in likelihood of dialysis in the patients initiating Soliris treatment post-transplant. In addition, 1 out of 53 patients who started on Soliris therapy before transplant required chronic dialysis, compared to 9 out of 65 patients who initiated Soliris treatment post-transplant, indicating a four-fold increase in the likelihood of chronic dialysis in patients initiating Soliris treatment post-transplant.

"The aim of this analysis was to evaluate the timing of eculizumab treatment and the need for dialysis in patients with aHUS who receive a kidney transplant," said lead study investigator, Dr. Siedlecki. "These results suggest that initiating treatment with eculizumab prior to kidney transplant, and maintaining treatment, reduces the risk of initiating dialysis after transplant in patients with a clinical diagnosis of aHUS."

The Global aHUS Registry is dedicated to increasing the knowledge of the natural history of aHUS, irrespective of management strategy, to help optimize care and improve quality of life for patients. Data from the registry serve to enhance the understanding of aHUS, as well as the use of Soliris as a treatment for patients with aHUS.

About Atypical Hemolytic Uremic Syndrome (aHUS)

aHUS is a chronic, ultra-rare, and life-threatening disease in which a life-long and permanent genetic deficiency in one or more complement regulatory genes causes chronic uncontrolled complement activation, resulting in complement-mediated thrombotic microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body.^{6,7} Permanent, uncontrolled complement activation in aHUS causes a life-long risk for TMA, which leads to sudden, catastrophic, and life-threatening damage to the kidney, brain, heart, and other vital organs, and premature death.^{7,8} Seventy-nine percent of all patients with aHUS die, require kidney dialysis or have permanent kidney damage within three years after diagnosis despite plasma exchange or plasma infusion (PE/PI).⁹ Moreover, 33-40 percent of patients die or progress to end-stage renal disease with the first clinical manifestation of aHUS despite PE/PI.^{9,10} The majority of patients with aHUS who receive a kidney transplant commonly experience subsequent systemic TMA, resulting in a 90 percent transplant failure rate in these TMA patients.¹¹

aHUS affects both children and adults. Complement-mediated TMA also causes reduction in platelet count (thrombocytopenia) and red blood cell destruction (hemolysis). While mutations have been identified in at least ten different complement regulatory genes, mutations are not identified in 40-50 percent of patients with a confirmed diagnosis of aHUS.^{9,11,12}

About Soliris® (eculizumab)

Soliris is a first-in-class terminal complement inhibitor developed from the laboratory through regulatory approval and commercialization by Alexion. Soliris is approved in the U.S. (2007), European Union (2007), Japan (2010) and other countries as the first and only treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis. PNH is a debilitating, ultra-rare and life-threatening blood disorder, characterized by complement-mediated hemolysis (destruction of red blood cells). Soliris is also approved in the U.S. (2011), European Union (2011), Japan (2013) and other countries as the first and only treatment for patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy, or TMA (blood clots in small vessels). aHUS is a debilitating, ultra-rare and life-threatening genetic disorder characterized by complement-mediated TMA. Soliris is not indicated for the treatment of patients with Shiga-toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS). For the breakthrough medical innovation in complement inhibition, Alexion and Soliris have received some of the pharmaceutical industry's highest honors: the Prix Galien USA (2008, Best Biotechnology Product) and France (2009, Rare Disease Treatment).

More information on Soliris, including the full U.S. prescribing information, is available at www.soliris.net.

IMPORTANT SAFETY INFORMATION:

The U.S. product label for Soliris includes a boxed warning: "Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early [see Warnings and Precautions (5.1)]. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies. Immunize patients with a meningococcal vaccine at least two weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. [See Warnings and Precautions (5.1) for additional guidance on the management of the risk of meningococcal infection]. Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected. Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program [see Warnings and Precautions (5.2)]. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or at www.solirisrems.com."

In patients with PNH, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, nasopharyngitis (runny nose), back pain and nausea. Soliris treatment of patients with PNH should not alter anticoagulant management because the effect of withdrawal of anticoagulant therapy during Soliris treatment has not been established. In patients with aHUS, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, and pyrexia. Soliris is not indicated for the treatment of patients with Shiga-toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS). Please see full prescribing information for Soliris, including BOXED WARNING regarding risk of serious meningococcal infection.

About Alexion

Alexion is a global biopharmaceutical company focused on developing and delivering life-transforming therapies for patients with devastating and rare disorders. Alexion is the global leader in complement inhibition and has developed and commercializes the first and only approved complement inhibitor to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), two life-threatening ultra-rare disorders. In addition, Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). Alexion is advancing the most robust rare disease pipeline in the biotech industry with highly innovative product candidates in multiple therapeutic areas. This press release and further information about Alexion can be found at: www.alexion.com.

[ALXN-G]

Forward-Looking Statements

This news release contains forward-looking statements, including statements related to potential medical benefits of Soliris® (eculizumab) for the treatment of atypical hemolytic uremic syndrome (aHUS). Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ from those expected, including for example, risks and uncertainties of drug development, decisions of regulatory authorities regarding marketing approval or material limitations on the marketing of Soliris for its current or potential new indications, delays in arranging satisfactory manufacturing capabilities for Soliris for aHUS, the possibility that results of clinical trials are not predictive of safety and efficacy results of Soliris in broader or different patient populations, the risk that third party payors (including governmental agencies) will not reimburse for the use of Soliris for the treatment of aHUS at acceptable rates or at all, the risk that estimates regarding the number of patients with aHUS and observations regarding the natural history of patients with aHUS are inaccurate, 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 June 30, 2016 and in our other filings with the U.S. 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. Siedlecki A, Isbel N, Vande Walle J, et al. Timing of Eculizumab Treatment and the Need for Dialysis in Patients with aHUS Who Receive a Kidney Transplant. Oral presentation at the American Society of Nephrology Annual Meeting, Chicago, November 19. Abstract TH-OR095.
2. Benz K, Amann K. Thrombotic microangiopathy: new insights. *Curr Opin Nephrol Hypertens*. 2010;19(3):242-247.
3. Ariceta G, Besbas N, Johnson S, et al. Guideline for the investigation and initial therapy of diarrhea-negative hemolytic uremic syndrome. *Pediatr Nephrol*. 2009;24:687-696.
4. Tsai HM. The molecular biology of thrombotic microangiopathy. *Kidney Int*. 2006;70(1):16-23.
5. Schaefer F, Fakhouri F, Kupelian V, et al. Age at Onset, Complement Abnormality and Renal Survival in Patients with aHUS Enrolled in a Global Registry. Poster presentation at the American Society of Nephrology Annual Meeting, Chicago, November 19. Abstract SA-PO783.
6. Benz K, Amann K. Thrombotic microangiopathy: new insights. *Curr Opin Nephrol Hypertens*. 2010;19(3):242-7.
7. Ariceta G, Besbas N, Johnson S, et al. Guideline for the investigation and initial therapy of diarrhea-negative hemolytic uremic syndrome. *Pediatr Nephrol*. 2009;24:687-96.
8. Tsai HM. The molecular biology of thrombotic microangiopathy. *Kidney Int*. 2006;70(1):16-23.
9. Noris M, Caprioli J, Bresin E, et al. Relative Role of genetic complement abnormalities in sporadic and familial aHUS and their impact on clinical phenotype. *Clin J Am Soc Nephrol*. 2010;5:1844-59.
10. Caprioli J, Noris M, Brioschi S, et al; for the International Registry of Recurrent and Familial HUS/TTP. Genetics of HUS: the impact of MCP, CFH, and IF mutations on clinical presentation, response to treatment, and outcome. *Blood*. 2006;108:1267-1279.
11. Bresin E, et al. Combined Complement Gene Mutations in Atypical Hemolytic Uremic Syndrome Influence Clinical Phenotype. *J Am Soc Nephrol*. 2013;24: 475-486.
12. Fremeaux-Bacchi, et al. Genetics and Outcome of Atypical Hemolytic Uremic Syndrome: A Nationwide French Series Comparing Children and Adults. *Clin J Am Soc Nephrol*. 2013 Apr 5; 8(4): 554-562.

View source version on [businesswire.com](http://www.businesswire.com/news/home/20161117006414/en/): <http://www.businesswire.com/news/home/20161117006414/en/>

Alexion Pharmaceuticals, Inc.

Media

Stephanie Fagan, 475-230-3777

Senior Vice President, Corporate Communications

or

Emily Vlasak, 475-230-3782

Associate Director, Corporate Communications

or

Investors

Elena Ridloff, CFA, 475-230-3601

Vice President, Investor Relations

Source: Alexion Pharmaceuticals, Inc.

News Provided by Acquire Media