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New Data Presented at the ERA-EDTA Congress Demonstrate Efficacy of Soliris® (eculizumab) in Broad Range of Patients with atypical Hemolytic Uremic Syndrome (aHUS)

- Improvements in Hematologic Markers of Complement-Mediated Thrombotic Microangiopathy (TMA) and Reversal of Renal Damage Reported in Patients With or Without a History of Renal Transplant or Dialysis -

- Additional Survival Analysis in Patients with aHUS Treated with Soliris and Biomarker Data Supporting the Need for Chronic Terminal Complement Blockade with Soliris Also Presented -

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq:ALXN) today announced that researchers presented data from clinical trials supporting the chronic use of Soliris® (eculizumab) in a broad range of patients with atypical hemolytic uremic syndrome (aHUS), a genetic, chronic, ultra-rare disease associated with vital organ failure and premature death. In a series of presentations at the 51st European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Congress in Amsterdam, The Netherlands, investigators reported the following results:

- In three separate subgroup analyses, treatment with Soliris resulted in clinically meaningful improvements in key hematologic markers of complement-mediated thrombotic microangiopathy (TMA) and reversal of renal damage in patients with aHUS, regardless of kidney transplant history or baseline dialysis status.[1-3]
- A survival analysis in patients with aHUS suggested that Soliris substantially reduced mortality, compared with model-derived predicted outcomes for patients who would have continued to receive only supportive care in two Soliris clinical trials.[4]
- Updated data from a study of key aHUS biomarkers demonstrated that, prior to Soliris treatment, patients with aHUS have severe ongoing terminal complement activation, complement-alternative pathway (CAP) activation, inflammation with increased thrombotic risk and severe renal damage. Blockade of terminal complement activity with Soliris treatment inhibited endothelial damage, inflammation, thrombotic risk and renal damage in these patients. Furthermore, during one year of Soliris treatment, markers of CAP activation and endothelial cell activation were reduced but persisted without clinical consequences, supporting the importance of sustained inhibition of terminal complement activation with Soliris to avoid potentially catastrophic clinical consequences of aHUS.[5]

"The subgroup analyses from our large prospective trials provide additional support that Soliris is effective in a broad group of patients with aHUS, consistently showing that chronic treatment with Soliris inhibited systemic complement-mediated TMA, reversed renal damage, and decreased or eliminated the need for dialysis," said Leonard Bell, M.D., Chief Executive Officer of Alexion. "These data, together with the survival model analysis and the biomarker findings in aHUS, reflect our ongoing commitment to providing optimal care for pediatric and adult patients with this genetic disorder."

aHUS is a genetic, chronic, ultra-rare disease that can progressively damage vital organs, leading to stroke, heart attack, kidney failure, and death.[6] The morbidities and premature mortality in aHUS are caused by chronic, uncontrolled activation of the terminal complement system, resulting in systemic TMA, the formation of blood clots in small blood vessels throughout the body.[7,8] Soliris, a first-in-class terminal complement inhibitor, specifically targets uncontrolled complement activation, and is the first and only approved treatment for patients with aHUS in the United States, European Union, Japan and other countries.

Soliris in Adult Patients with aHUS, with or without a History of Kidney Transplant (Abstract MO013)

In an oral presentation today, Fadi Fakhouri M.D., Ph.D., of Centre Hospitalier Universitaire de Nantes in Nantes, France, reported that Soliris treatment resulted in clinically meaningful improvements in hematologic markers of complement-mediated TMA and reversal of renal damage in non-transplant patients (N=32) as well as in those with a history of kidney transplant (N=9), and that most patients were able to discontinue dialysis and remain dialysis-free. In this sub-analysis of a large, prospective open-label, single-arm study of Soliris in adult patients with aHUS, researchers reported that, of the patients who were on dialysis at baseline, 18 of the 21 (86%) non-transplant patients and two of the three (67%) transplant patients discontinued dialysis. The mean change in platelet count from baseline was 132.6 x 10^9/L (standard deviation [SD] 110.6; $p < 0.0001$) in non-transplant patients and 146.2 x 10^9/L (SD 140.8; $p=0.0810$) in transplant patients at 26 weeks of Soliris treatment. The mean change from baseline in estimated glomerular filtration rate (eGFR), a measure of kidney function, was 31.5 mL/min/1.73m^2 (SD 22.8; $p < 0.0001$) in non-transplant patients and 19.0 mL/min/1.73m^2 (SD 27.3; $p=0.1940$) in transplant patients. The study authors concluded that recovery of kidney function was more modest in patients with

transplanted kidneys, highlighting the greater risk of, and therefore need to prevent, new TMA manifestations in patients with aHUS who have a history of kidney transplant. In addition, the study highlights the importance of early initiation with Soliris for patients with native kidneys to prevent progression to end-stage renal disease (ESRD) and transplant. Soliris was well tolerated in both groups and the treatment-emergent adverse event (TEAE) profile was similar for both groups.[1]

"In this subgroup analysis, Soliris treatment led to inhibition of complement-mediated TMA, resulting in substantial recovery of kidney function for both non-transplant and transplant patients with aHUS," noted Dr. Fakhouri. "These data provide additional support demonstrating the clinical benefit of chronic Soliris treatment in both non-transplant and transplant patients with aHUS."

Soliris in Adult Patients with aHUS, with or without Dialysis at Baseline (Abstract SP286)

A separate sub-analysis of the same study reported above focused on adult patients with and without a history of dialysis at baseline (N=24 and N=17, respectively), and showed that Soliris significantly improved hematologic markers of complement-mediated TMA and reversed renal damage in both subgroups. As presented by Dr. Fakhouri in a poster session on June 1, Soliris significantly improved platelet count in patients with dialysis at baseline (mean [SD] change from baseline: 163.2 [120.0] x 10^9/L; $p < 0.0001$) as well as in those without dialysis at baseline (87.4 [88.2] x 10^9/L; p=0.0120). Soliris also significantly improved mean (SD) eGFR from baseline by 35.0 (22.3) mL/min/1.73m^2 in the dialysis group ($p < 0.0001$) and by 20.0 (23.5) mL/min/1.73m^2 in the non-dialysis group (p=0.0179). Of the 24 patients on dialysis at baseline, 20 (83.3%) discontinued dialysis during the 26-week study period, and none needed to resume dialysis. Although four patients without a history of dialysis at baseline required new dialysis during Soliris treatment, two of these patients were able to discontinue a short course of dialysis by week 26. Soliris was well tolerated in both groups; rates of adverse events were similar in both groups and no new or unexpected safety concerns were reported. The totality of the data collected provide further support that patients on dialysis benefit from early Soliris treatment, and early initiation with Soliris provides a clinical benefit in adult patients with aHUS with and without a history of dialysis.[2]

Soliris in Pediatric Patients with aHUS, with or without Dialysis at Baseline (Abstract SP281)

In another poster presentation on June 1, Johan Vande Walle, M.D., Ph.D., of the University of Ghent, Belgium, reported on a sub-analysis from a large, prospective, open-label, single-arm study designed to characterize the safety and efficacy of Soliris in pediatric patients with aHUS (aged 1 month to 18 years) with (N=11) and without (N=11) dialysis at baseline. Treatment with Soliris resulted in clinically meaningful improvements in hematologic markers of complement-mediated TMA and reversed renal damage in both groups. Specifically, Soliris treatment improved platelet count both in the dialysis group (mean [SD] change from baseline: 149.8 [101.0] x 10^9/L; p=0.0150) and in the non-dialysis group (180.2 [34.9] x 10^9/L; p=0.0003). Increases in eGFR were also observed for both the dialysis (mean [SD] change from baseline: 57.7 [57.3] mL/min/1.73m^2; p=0.0568) and non-dialysis (70.3 [37.1] mL/min/1.73m^2; p=0.0056) groups. Of the 11 patients on dialysis at baseline, nine (82%) discontinued dialysis by 26 weeks, and of the 11 patients not on dialysis at baseline, all 11 (100%) remained dialysis-free during and at 26 weeks. Soliris was well tolerated in both groups and the TEAE profile was similar for both groups.[3]

Survival Analysis in Patients with aHUS (Abstract SP606)

A separate poster presented on June 1 compared outcomes in patients with aHUS receiving Soliris in the aHUS registration trials[9] to the predicted outcomes for these same clinical trial participants had they continued to receive only supportive care based on statistical and clinical modeling. The predictive data were derived from a Markov model that was developed to estimate the mortality rate of patients with aHUS based on the patient's decline of renal function prior to Soliris treatment, time to ESRD, likelihood of death conditional on receiving chronic dialysis, and estimated non-renal excess mortality rate from aHUS. In this study, the Markov model tracked patients' progression through three CKD stages (CKD 0-2, CKD 3a-4, or CKD 5 [or ESRD]), plus transplant and death.[4]

The model estimated an 8.1%, 16.2% and a 24.3% mortality rate at one, two and three years, respectively, for patients with aHUS receiving supportive care, which is consistent with the literature-reported mortality observed in three large aHUS and TMA registries. [7,10,11] There was one reported death during Soliris treatment (deemed unrelated to the study drug) with a median follow-up time of 37 months, resulting in a 1.4% annual mortality rate with Soliris. Soliris reduced the risk of mortality by 89% at three years (with relative risk 11% [95% CI: 1%-83%; p=0.0138]), compared to the same patients if they had continued to receive only supportive care.[4] This analysis demonstrates a persistent risk of vital organ failure and mortality in patients with aHUS, indicating the need for chronic terminal complement inhibition with Soliris.

Biomarkers in Patients with aHUS Treated with Soliris (Abstract MP035)

In a poster session today, researchers presented updated biomarker data from a prospective open-label trial of adult patients with aHUS treated with Soliris.[5] Building on data previously reported at the 2013 annual meeting of the American Society of

Hematology[12], the researchers presented an analysis of biologic measures of complement-mediated TMA by genetic mutational status. At baseline, markers of CAP activation, endothelial cell activation and damage, inflammation, coagulation and renal damage were all significantly elevated above normal levels in patients with aHUS, regardless (1) of presence of identified mutations, (2) if patients received PE/PI or (3) had normal platelet count at baseline. During inhibition of terminal complement activity with Soliris, terminal complement and renal damage marker levels normalized and markers of endothelial cell damage, inflammation and coagulation were reduced to near-normal levels, demonstrating that progressive endothelial and renal damage are driven by over-activation of terminal complement. Further, endothelial activation and CAP activity (upstream of the terminal complement pathway) remained significantly elevated among patients treated with Soliris, demonstrating that patients with aHUS have ongoing unregulated CAP activity. Taken together, patients with aHUS continue to show ongoing proximal complement activity but the mechanisms for TMA and organ damage are determined by terminal complement activation. These data support the importance of sustained inhibition of terminal complement activation with Soliris to avoid potentially catastrophic clinical consequences.[5]

"The data from this study show that markers of the alternative complement activation pathway and endothelial cell activation are reduced with Soliris treatment but remain elevated in patients with aHUS," said Camille L. Bedrosian, M.D., Chief Medical Officer of Alexion. "The results underscore the chronic complement dysregulation and ongoing risk of systemic TMA and organ damage in patients with aHUS, and the requirement for continued terminal complement blockade with Soliris, even when clinical presentation and clinical laboratory values have improved."

About aHUS

aHUS is a chronic, ultra-rare, and life-threatening disease in which a 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.[13,14] 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.[13,15] Sixty-five percent of all patients with aHUS die, require kidney dialysis, or have permanent kidney damage within the first year after diagnosis despite plasma exchange or plasma infusion (PE/PI).[8,16] The majority of patients with aHUS who receive a kidney transplant commonly experience subsequent systemic TMA, resulting in a 90% transplant failure rate in these TMA patients.[17]

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 30-50% of patients with a confirmed diagnosis of aHUS.[7]

About Soliris® (eculizumab)

Soliris® (eculizumab) 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), a debilitating, ultra-rare and life-threatening blood disorder, characterized by complement-mediated hemolysis (destruction of red blood cells). Soliris is indicated to reduce hemolysis in PNH patients. Soliris is also approved in the U.S. (2011), the European Union (2011), Japan (2013) and other countries as the first and only treatment for patients with atypical hemolytic uremic syndrome (aHUS), a debilitating, ultra-rare and life-threatening genetic disorder characterized by complement-mediated thrombotic microangiopathy, or TMA (blood clots in small vessels). The effectiveness of Soliris in aHUS is based on the effects on TMA and renal function. Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS). More information, including the full prescribing information on Soliris, 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 2 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)."

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, 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. http://soliris.net/sites/default/files/assets/soliris_pi.pdf

About Alexion

Alexion is a biopharmaceutical company focused on serving patients with severe and rare disorders through the innovation, development and commercialization of life-transforming therapeutic products. Alexion is the global leader in complement inhibition and has developed and markets Soliris® (eculizumab) as a treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is currently approved in nearly 50 countries for the treatment of PNH and aHUS. Alexion is evaluating other potential indications for Soliris in additional severe and ultra-rare disorders beyond PNH and aHUS, and is developing other highly innovative biotechnology product candidates, including asfotase alfa, across multiple therapeutic areas. This press release and further information about Alexion 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, regulatory and commercial 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, 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, 2014, 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.

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Alexion Pharmaceuticals, Inc.
Media:
Irving Adler, 203-271-8210
Executive Director, Corporate Communications
or
Kim Diamond, 203-439-9600
Senior Director, Corporate Communications
or
Investors:
Elena Ridloff, 203-699-7722
Executive Director, Investor Relations

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