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Long-Term Follow-up Study Presented at ASN 2015 Supports Effectiveness of Soliris® (eculizumab) in Preventing Thrombotic Microangiopathy (TMA) Events in Patients with Atypical Hemolytic Uremic Syndrome (aHUS)

- Updated 1-Year Data from Phase 2 Study of Eculizumab in Prevention of Acute Antibody-Mediated Rejection (AMR) in Sensitized Deceased-Donor Kidney Transplant Recipients Also Reported -

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced that researchers presented new data from a long-term follow-up study evaluating the effectiveness and safety of Soliris® (eculizumab) in preventing thrombotic microangiopathy (TMA)—the formation of blood clots in small blood vessels throughout the body—in patients with atypical hemolytic uremic syndrome (aHUS), a genetic, chronic, ultra-rare disease associated with vital organ failure and premature death.[1,2,3] In this observational study, researchers reported a 74 percent lower TMA event rate with ongoing Soliris treatment with labeled dosing compared with discontinuation of Soliris therapy.[4] These data were presented at the 2015 American Society of Nephrology (ASN) Annual Meeting in San Diego.

"Patients with aHUS face a life-long risk of unpredictable TMA events, which can lead to catastrophic damage to vital organs and premature death. Data from the long-term follow-up study presented at ASN underscore the importance of continuous, on-label treatment with Soliris in reducing the rate and severity of TMA events in patients with aHUS," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "Four years after the launch of Soliris for the treatment of aHUS, these findings provide important insight into the long-term clinical benefits of ongoing terminal complement inhibition with Soliris."

Additionally, in a late-breaking poster session at ASN, researchers reported updated 1-year results from an open-label, single-arm Phase 2 trial of eculizumab in the prevention of acute antibody-mediated rejection (AMR) in sensitized deceased-donor kidney transplant recipients.[5] Acute AMR is a serious and potentially life-threatening condition that can lead to severe allograft damage resulting in rapid loss of function and possible loss of the transplanted organ.[6]

Additional studies presented at ASN included a post-hoc analysis evaluating the safety of Soliris in pediatric and adolescent patients with aHUS and an update from the Global aHUS Registry.

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. Soliris is not approved in any country for the prevention or treatment of AMR.

Eculizumab Prevents Thrombotic Microangiopathy in Atypical Hemolytic Uremic Syndrome Patients: Long-Term Follow-up (FR-PO446)[4]

Jan Menne, M.D., of Hannover Medical School, Hannover, Germany, presented results from an ongoing, long-term follow-up study evaluating the rate and severity of TMA events during treatment with Soliris and following discontinuation of Soliris treatment in patients with aHUS. The study included 87 patients who had been treated with Soliris in any of five previous clinical studies. Seventy-six patients had on-treatment periods (median 45.9 months) and 39 patients had off-treatment periods (median 20.1 months) during this observational trial.

For the primary endpoint, researchers reported that the TMA event rate was 63 percent lower during periods of Soliris treatment compared to periods of treatment discontinuation. Additionally, the rate of TMA events during periods of on-label dosing of Soliris was 74 percent lower than during periods of treatment discontinuation, and was also 57 percent lower compared with periods when patients were on treatment but receiving non-labeled dosing. Moreover, off-treatment periods were more frequently associated with serious adverse events and hospitalizations related to TMA events compared with on-treatment periods.

There were no unexpected safety signals reported during the observational study period, and treatment-emergent adverse event rates were similar between the two groups. One adult patient from parent study C10-004 died during the observational study due to intensive care complications and multi-organ failure determined to be caused by coexisting disease and unrelated to Soliris. Two patients from parent study C09-001 reported meningococcal infections during the observational study; both were

determined to be probably related to Soliris. Both patients recovered and no changes to Soliris dosing were made.

"Reducing the severity and overall occurrence of TMA events and related complications is a primary objective in the management of patients with aHUS. Findings from this study, which demonstrated a significantly lower TMA event rate with Soliris treatment—particularly when on-label dosing was followed—compared with treatment discontinuation, reinforce the recommendation for long-term Soliris treatment reflected in the prescribing information to reduce the ongoing risk of TMA complications in patients with aHUS," said Jan Menne, M.D.

Eculizumab in Prevention of Acute Antibody-Mediated Rejection in Sensitized Deceased-Donor Kidney Transplant Recipients: Updated 12-Month Outcomes (SA-PO1122)[5]

In a late-breaking poster session, Denis Glotz, M.D., Ph.D., of Hôpital Saint-Louis, Paris, presented updated 1-year results from the ongoing open-label, multicenter, single-arm Phase 2 study of eculizumab in the prevention of acute AMR in sensitized deceased-donor kidney transplant recipients. Researchers reported that post-transplant failure occurred in 22.5 percent of patients (18/80) at 1 year, including a 12.5 percent incidence of AMR, based on locally read biopsies. Graft and patient survival at 1 year were 88.7 percent and 97.4 percent, respectively.[5] The preliminary results presented at ASN were based on local biopsy data; a central read of the biopsy data is ongoing as required for the pre-specified primary endpoint of this study.

No new safety signals were identified in this study. Through 1 year, the most common treatment-emergent serious adverse events were transplant rejection (28.8 percent), complications of the transplanted kidney (15.0 percent), and acute renal failure (12.5 percent). Two patients (2.5 percent) in the study died, one due to multi-organ failure and one due to proximal small bowel perforation, both deemed not related to eculizumab.

"Acute AMR is a serious and potentially life-threatening complication that can lead to significant negative outcomes in transplanted patients and can pose a barrier to transplantation in sensitized patients waiting to receive a kidney," said Denis Glotz, M.D., Ph.D. "Findings from this single-arm study suggest that eculizumab may be effective in reducing the incidence of acute AMR in sensitized deceased-donor kidney transplant recipients, with outcomes similar to those expected for non-sensitized patients."

Safety of Eculizumab in Pediatric Patients with Atypical Hemolytic Uremic Syndrome (TH-PO460)[7]

Gema Ariceta, M.D., Ph.D., of the Hospital Universitario Materno-Infantil Vall d'Hebron, Barcelona, presented a post-hoc analysis of safety data from three prospective clinical trials in 28 pediatric (< 12 years of age) and adolescent (12-17 years of age) patients with aHUS treated with Soliris.

Most treatment-emergent adverse events (TEAEs) reported in the analysis were mild to moderate in severity. Of the patients experiencing TEAEs, half (n=13) had events determined to be at least possibly related to Soliris (TRAEs). The most common TRAEs reported by 1 year of Soliris treatment were skin/subcutaneous tissue disorders including alopecia, dermatitis, eczema, erythema and rash, and infections/infestations including ear infection, fungal infection, nasopharyngitis, and oral fungal infection. Four patients reported serious TRAEs by 1 year of treatment, including infections and agitation. By end of study (mean 67 weeks), 6 infection-related serious TRAEs occurred in 4 patients, including viral upper respiratory tract infection (n=2), influenza peritonitis, respiratory syncytial virus infection, and pyelonephritis (n=1 each).

No unexpected TRAEs were noted and no deaths or meningococcal infections were reported. Although infections were the most commonly observed TRAEs, most were mild to moderate in severity and expected in a pediatric population, none led to treatment discontinuation, and all patients recovered. Researchers concluded that treatment with Soliris is well tolerated in pediatric patients with aHUS, with a safety profile consistent with the broader patient population of the clinical trial program.

Characteristics of 681 Adult and Pediatric Patients in the Global aHUS Registry (FR-PO483)[8]

Christoph Licht, M.D., FASN, of The Hospital for Sick Children, Toronto, presented baseline demographics from 681 patients in the Global aHUS Registry. The evaluation of baseline characteristics revealed that adult patients with aHUS (> 18 years of age) experienced more than double the rate of thrombosis events than pediatric patients with aHUS (< 18 years of age) (14.1 percent vs 6.2 percent) between aHUS diagnosis and baseline. The vast majority of both adult and pediatric patients experienced at least one TMA event beyond their diagnosis event and before baseline. Extra-renal complications also occurred commonly in both age groups. The aHUS Registry is dedicated to increasing the understanding and awareness of aHUS to help optimize care and improve quality of life for patients.

About 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.[1,2] 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.[1,3] 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 to 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 30-50 percent of patients with a confirmed diagnosis of aHUS.[9]

About Acute Antibody-Mediated Rejection (AMR)

Acute AMR is a severe and potentially life-threatening condition that can lead to severe allograft damage resulting in rapid loss of function and possible loss of the transplanted organ.[6] Patients who are sensitized (have high levels of donor-specific-antibodies [DSAs]) are at high risk for developing acute AMR.[6,12] The historical rate of acute AMR in high-risk living-donor kidney transplant recipients has been reported as high as 41 percent.[13] Acute AMR is believed to be primarily a result of uncontrolled complement activation caused by DSAs.[6,12] Currently, there are no approved therapies for the prevention or treatment of acute AMR.

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, including the full U.S. 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 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)."

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 developed and commercializes Soliris® (eculizumab), 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. As the global leader in complement inhibition, Alexion is strengthening and broadening its portfolio of complement inhibitors, including evaluating potential indications for eculizumab in additional severe and ultra-rare disorders. Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, Strensiq™ (asfotase alfa) to treat patients with hypophosphatasia (HPP) and Kanuma™ (sebelipase alfa) to treat patients with lysosomal acid lipase deficiency (LAD). In addition, 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.

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Forward-Looking Statements

This news release contains forward-looking statements, including statements related to potential medical benefits of Soliris® (eculizumab) in atypical hemolytic uremic syndrome (aHUS) and acute antibody-mediated rejection (AMR). 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, 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, 2015 and Alexion's other filings with the SEC. 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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