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Researchers Present New Data from Phase 2 Clinical Trial of Eculizumab (Soliris®) in Prevention of Acute Antibody-Mediated Rejection (AMR) in Sensitized Deceased-Donor Kidney Transplant Recipients

- Preliminary Data Presented at 2015 American Transplant Congress (ATC) -

- Additional Studies Presented at ATC Illustrate Burden of Disease in AMR and Explore Role of Complement in Delayed Graft Function (DGF) -

- Researchers Also Present Longer-Term Data Underscoring Clinical Benefits of Ongoing Soliris Therapy in Adult Patients with Atypical Hemolytic Uremic Syndrome (aHUS) with or without History of Transplant -

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced that researchers presented preliminary 1-year data from a single-arm Phase 2 study of eculizumab (Soliris®) in the prevention of acute antibody-mediated rejection (AMR) in sensitized deceased-donor kidney transplant recipients. 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.[1] In a late-breaking oral session today, researchers reported that the composite efficacy endpoint of post-transplant treatment failure occurred in 18.8% of patients (15/80) at 1 year, with a 10% incidence of AMR, in this ongoing, open-label study. Graft and patient survival at 1 year were 87.1% and 97.4%, respectively.[2]

These data were presented at the 2015 American Transplant Congress (ATC) in Philadelphia, where researchers also presented the following:

- Late-breaking data from a burden-of-disease study in which AMR development was associated with greater resource utilization and significantly higher post-transplant costs compared to patients who did not develop AMR[3]
- Data from a non-clinical animal-model study providing support that the terminal complement pathway plays an important role in the development of delayed graft function (DGF) following kidney transplantation[4]
- Data from a post-hoc sub-analysis from a prospective, open-label, single arm trial of Soliris in adult patients with atypical hemolytic uremic syndrome (aHUS) in which an increased percentage of patients experienced improvements in hematologic and renal outcomes with longer-term Soliris treatment, regardless of transplant history[5]

"The data presented at the 2015 American Transplant Congress enhance our understanding of AMR and DGF, two serious and potentially life-threatening complications of kidney transplantation. We continue to advance the development of eculizumab in these settings to address the significant barriers to transplantation and burden of disease that the community currently faces," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "Separately, the aHUS data presented today further underscore the clinical benefits of ongoing Soliris therapy in adult patients with aHUS, irrespective of transplant history."

Soliris is a first-in-class terminal complement inhibitor approved in nearly 50 countries as a treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH) and in nearly 40 countries as a treatment for patients with aHUS. Both PNH and aHUS are life-threatening ultra-rare diseases caused by chronic uncontrolled complement activation. Soliris is not approved in any country for the prevention or treatment of AMR or DGF.

The following data were presented at the 2015 ATC:

Eculizumab in Prevention of Acute Antibody-Mediated Rejection in Sensitized Deceased-Donor Kidney Transplant Recipients: 1-Year Outcomes (Abstract 3039)

In a late-breaking oral session, Denis Glotz, M.D., Ph.D., Chief of the Department of Nephrology and Transplantation at Hôpital Saint-Louis, Paris, presented 1-year results from an open-label, single-arm, multicenter Phase 2 trial (N=80) evaluating the safety and efficacy of eculizumab in the prevention of acute AMR in sensitized deceased-donor kidney transplant recipients. Preliminary nine-week data from this study were reported at the European Society for Organ Transplantation (ESOT) Annual Congress in 2013.[6]

Dr. Glotz today reported preliminary 1-year outcomes from this ongoing trial, which is now fully enrolled. The composite efficacy endpoint of week 9 post-transplant failure, defined as biopsy-proven AMR, graft loss, patient death, or loss to follow-up, occurred in 12.5% (10/80) of patients, with a 7.5% rate of AMR (6/80) based on locally read biopsies, compared with the historical 30% rate of AMR expected with best available care in this highly sensitized population.[2,7] At 1 year, post-transplant failure occurred in 18.8% (15/80) of patients, including a 10.0% incidence of AMR (8/80) based on locally read biopsies. Graft and patient survival at 1 year were 87.1% and 97.4%, respectively. The preliminary results presented at ATC were based on local laboratory data; a central read of the laboratory data is ongoing as required for the pre-specified primary endpoint of this study. Mean creatinine levels were 7.44 mg/dL (n=78) and 1.80 mg/dL (n=45) at baseline and 1 year, respectively.[2]

No new safety signals were identified in this study. At 1 year, the most common treatment-emergent serious adverse events were transplant rejection (26.3%), acute renal failure (13.8%) and complications of the transplanted kidney (10.0%). Two patients (2.5%) in the study died, one due to multi-organ failure and one due to proximal small bowel perforation, both deemed not related to eculizumab. [2]

"Acute AMR is a significant clinical barrier to transplantation in sensitized patients, who make up approximately 60% of the transplant waiting list and currently have no approved options available to address this severe and potentially life-threatening risk," said Dr. Glotz. "While we recognize the limitations of the single-arm study design and the need for further exploration, the findings suggest that eculizumab may be effective in reducing the incidence of acute AMR in sensitized deceased-donor kidney transplant patients, with rates of graft survival, patient survival and kidney function at 1 year that were similar to those expected for non-sensitized kidney transplant recipients."

Burden of Early Antibody-Mediated Rejection (AMR) (Poster A296)

In a late-breaking poster session, Ramandeep S. Banga, M.D., of the Mayo Clinic, Rochester, presented results from a retrospective study that assessed complications, resource utilization and costs of acute AMR (up to 1 year post-transplant) in adult patients (N=48; 21 with AMR, 27 without AMR) with high levels of donor-specific antibody who underwent kidney transplantation.

In the study, acute AMR was associated with higher rates of resource utilization, including hospital days (24.3 vs. 12.9, p=0.014), plasma exchange sessions (20.38 vs. 11.04, p=0.003), renal biopsies (5.9 vs. 3.6, p < 0.001), IVIG doses (17.9 vs. 10.3, p=0.02), and more surgical procedures, including splenectomy and wound dehiscence. In addition, while pre-transplant costs were similar between the groups, AMR was associated with significantly higher post-transplant costs ($159,705 vs. $94,352; p=0.02). No significant difference in rates of medical and surgical complications was observed between the two groups.[3]

Targeting Complement Pathways during Ischemia and Reperfusion: Implications for the Prevention of Delayed Graft Function (Abstract 789)

In an oral session, Alexion researcher Zhao-Xue Yu, Ph.D, M.D., presented data from a nonclinical study that evaluated the effects of inhibiting the complement alternative pathway and terminal pathway during cold ischemia and reperfusion of the kidney on the development of DGF in a rat model of kidney transplantation. DGF is an early and serious complication of organ transplantation characterized by the failure of a transplanted organ to function normally immediately following transplantation.

Researchers concluded that in this animal model, blockade of the terminal pathway improved graft function and survival, and may effectively protect against ischemia-reperfusion injury and subsequent DGF.[4]

1-Year Safety and Efficacy of Eculizumab in Adult aHUS Patients, With or Without a History of Renal Transplant (Abstract 1243)

In an oral session, Christophe M. Legendre, M.D., of the Université Paris Descartes and Hôpital Necker, Paris, presented a post-hoc sub-analysis from the C10-004 study that evaluated the safety and efficacy of Soliris at 26 weeks and 1 year in adult patients with aHUS (n=41) with and without a history of renal transplant.

As previously reported at the American Society of Nephrology meeting in 2014, at 26 weeks, the primary endpoint of complete TMA response—defined as platelet count normalization, LDH normalization and preservation of renal function—was achieved in 78% (25/32) of non-transplant patients and in 56% (5/9) of transplant patients. At 1 year, complete TMA response was achieved in a greater proportion of patients: 84% (27/32) of non-transplant patients and 67% (6/9) of transplant patients. Dr. Legendre also reported that[5]:

- At 26 weeks, 97% (31/32) of non-transplant and 100% (9/9) of transplant patients achieved platelet count normalization compared with 100% (32/32) of non-transplant and 100% (9/9) of transplant patients at 1 year

- At 26 weeks, 94% (30/32) of non-transplant and 78% (7/9) of transplant patients achieved LDH normalization, compared with 100% (32/32) of non-transplant and 89% (8/9) of transplant patients at 1 year
- At 26 weeks, 56% (18/32) of non-transplant and 44% (4/9) of transplant patients achieved eGFR improvement from baseline of ≥15 mL/min/1.73 m^2 compared with 66% (21/32) of non-transplant and 44% (4/9) of transplant patients at 1 year
- 86% of non-transplant and 67% of transplant patients discontinued dialysis by week 26. All patients who discontinued dialysis remained dialysis-free at 1 year, and none progressed to end-stage renal disease or required a subsequent graft

"In this 1-year analysis, we observed that ongoing treatment with Soliris continued to inhibit complement-mediated TMA and led to improvements in platelet count and renal function that were achieved by a greater percentage of patients at 1 year. These gains were more significant in patients with native kidney than in those who were transplanted," said Dr. Legendre. "Importantly, in a population of transplanted patients with a historically very high risk of graft loss, no new patients treated with Soliris in this study lost their graft at 1 year."

There were no unexpected adverse events reported during the 1-year analysis period. As previously described, two patients in the C10-004 study developed meningococcal infections (one patient discontinued from the study and later recovered; the other continued treatment with no interruption and recovered without sequelae). The most common AEs reported by sub-group at 1 year were: for patients with renal transplant, diarrhea (66.7%), anemia (44.4%), urinary tract infection (33.3%), bronchitis (33.3%) and hematoma (33.3%); for patients without renal transplant, headache (40.6%), peripheral edema (28.1%), diarrhea (25.0%), nasopharyngitis (21.9%), cough (21.9%), and pyrexia (21.9%).[5]

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.[1] Patients who are sensitized (have high levels of donor-specific-antibodies [DSAs]) are at high risk for developing acute AMR.[1,8] The historical rate of acute AMR in high-risk living-donor kidney transplant recipients has been reported as high as 41%.[9] Acute AMR is believed to be primarily a result of uncontrolled complement activation caused by DSAs.[7,8] Currently, there are no approved therapies for the prevention or treatment of acute AMR.

About Delayed Graft Function (DGF)

DGF is an early and serious complication of organ transplantation that affects approximately 25 to 50 percent of deceased-donor kidney transplant cases and is characterized by the failure of a transplanted organ to function normally immediately following transplantation.[10,11] When DGF occurs in the setting of kidney transplantation, the patient requires dialysis after the transplant procedure.[11-13] Most often, DGF results from organ injury caused by severe inflammation and complement activation associated with the normal processes for removal, storage, and transplantation of the donor organ.[11-14] DGF has a substantial negative impact on graft function both in the short and long term, which can result in premature graft loss, prolonged hospitalization or patient death.[16,17] In addition, as donor organs are in short supply, reducing the risk of DGF for organs that are at higher risk to develop DGF may allow more donor organs to be transplanted. With specific regard to kidney transplantation, 15-20 percent of donor kidneys are reportedly never used and thus discarded each year in the U.S. and Europe due to the risk of poor outcomes associated with DGF[18,19], denying many patients the benefit of transplantation.

Currently, there are no approved therapies to prevent or treat DGF after kidney transplantation. For information about ongoing clinical trials such as the **PROTECT** (**PR**eventi**O**n of delayed graf**T** function using **EC**ulizumab **T**herapy) Study, visit clinicaltrials.gov, identifier NCT02145182.

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.[20,21] 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.[20,22] 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).[23] 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.[23,24] 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.[25]

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.[23]

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, 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 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 in nearly 40 countries for the treatment of 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.alexion.com.

Safe Harbor

This news release contains forward-looking statements, including statements related to potential medical benefits of Soliris (eculizumab) in acute antibody-mediated rejection (AMR), delayed graft function (DGF) and 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, 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, 2015. 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.

[ALXN-G]

References

1. Takemoto SK, Zeevi A, Feng S, et al. National conference to assess antibody-mediated rejection in solid organ transplantation. Am J Transplant. 2004; 4(7):1033-41.

2. Glotz, D, Russ G, Rostaing L, et. al. Eculizumab in prevention of acute antibody-mediated rejection in sensitized deceased-donor kidney transplant recipients: 1-year outcomes. Oral presented at the 2015 American Transplant Congress (ATC), Philadelphia, May 5. Abstract 3039.

3. Banga R, Schinstock C, Boscoe A, et. al. Burden of early antibody-mediated rejection (AMR): complications, resource utilization and cost-differential in treatment of AMR. Poster presented at the 2015 American Transplant Congress (ATC), Philadelphia, May 2. Abstract 3017.

4. Yu ZX, Qi S, Lasaro M, Bouchard K, et. al. Targeting complement pathways during ischemia and reperfusion: implications for the prevention of delayed graft function. Oral presented at the 2015 American Transplant Congress (ATC), Philadelphia, May 4. Abstract 789.

5. Legendre C, Kincaid J, Bedrosian C, et. al. 1-year safety and efficacy of eculizumab in adult aHUS patients, with or without a history of renal transplant. Oral presented at the 2015 American Transplant Congress (ATC), Philadelphia, May 5. Abstract 1243.

6. Glotz D, Legendre C, Manook M, et al. Eculizumab decreases early antibody-mediated rejection in sensitized deceased donor kidney transplant patients. Presented at the 2013 Congress of the European Society for Organ Transplantation (ESOT), Vienna, Austria, September 10, 2013.

7. LeFaucher C, Loupy A, Hill GS, et al. Preexisting donor-specific HLA antibodies predict outcome in kidney transplantation. J Am Soc Nephrol. 2010;21:1398-1406.

8. Collins AB, Schneeberger EE, Pascual MA, et al. Complement activation in acute humoral renal allograft rejection: diagnostic significance of C4d deposits in peritubular capillaries. J Am Soc Nephrol. 1999;10(10):2208-14.

9. Stegall MD1, Diwan T, Raghavaiah S, et al. Terminal complement inhibition decreases antibody-mediated rejection in sensitized renal transplant recipients. Am J Transplant. 2011 Nov;11(11):2405-13.

10. Irish WD, Ilsley JN, Schnitzler MA, Feng S, Brennan DC. A risk prediction model for delayed graft function in the current era of deceased donor renal transplantation. Am J Transplant. 2010;10(10):2279-86.

11. Yarlagadda SG, Coca SG, Garg AX, et al. Marked variation in the definition and diagnosis of delayed graft function: a systematic review. Nephrol Dial Transplant. 2008;23:2995-3003.

12. Jayaram D, Kommareddi M, Sung RS, Luan FL. Delayed graft function requiring more than one-time dialysis treatment is associated with inferior clinical outcomes. Clin Transplant. 2012;26(5):E536-43.

13. Siedlecki A, Irish W, Brennan DC. Delayed graft function in the kidney transplant. Am J Transplant. 2011;11:2279-96.

14. Perico N, Cattaneo D, Sayegh MH, Remuzzi G. Delayed graft function in kidney transplantation. Lancet. 2004;364:1814-27.

15. Yarlagadda SG, Klein CL, Jani A. Long-term renal outcomes after delayed graft function. Adv Chronic Kidney Dis. 2008;15:248-56.

16. Butala NM, Reese PP, Doshi MD, Parikh CR. Is delayed graft function causally associated with long-term outcomes after kidney transplantation? Instrumental variable analysis. Transplantation. 2013;95:1008-14.

17. Yarlagadda SG, Coca SG, Formica RN Jr, Poggio ED, Parikh CR. Association between delayed graft function and allograft and patient survival: a systematic review and meta-analysis. Nephrol Dial Transplant. 2009;24:1039-47.

18. US Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients. OPTN/SRTR Annual Report, 2009. Chapter II: Organ donation and utilization in the United States, 1999-2008. http://www.ustransplant.org/annual_reports/current/.

19. Eurotransplant. Statistics Report Library; 2013. http://statistics.eurotransplant.org/.

20. Benz K, Amann K. Thrombotic microangiopathy: new insights. Curr Opin Nephrol Hypertens. 2010;19(3):242-7.

21. 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.

22. Tsai HM. The molecular biology of thrombotic microangiopathy. Kidney Int. 2006;70(1):16-23.

23. Noris M, Remuzzi G. Atypical hemolytic-uremic syndrome. N Engl J Med. 2009;361:1676-87.

24. Caprioli J, Noris M, Brioschi S, et al. The impact of MCP, CFH, and IF mutations on clinical presentation, response to treatment, and outcome. Blood. 2006;108:1267-1269.

25. Bresin E, Daina E, Noris M, 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;1:88-99.

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