



Study Evaluating Eculizumab (Soliris®) in Preventing Antibody-Mediated Rejection (AMR) in Kidney Transplant Recipients Presented at the European Society for Organ Transplantation (ESOT) Annual Congress

September 10, 2013

—Preliminary Data Show Potential for Effective Prophylaxis Against Early Acute AMR in Deceased-Donor Kidney Transplant Recipients Highly Sensitized to Their Donors —

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) today announced that researchers have presented preliminary data from a single-arm Phase 2 study of eculizumab (Soliris®) as an investigational therapy to prevent acute antibody-mediated rejection (AMR) in sensitized deceased-donor kidney transplant recipients. The composite primary endpoint was the nine-week occurrence of post-transplantation treatment failure, which occurred in 10.6% of the 47 patients reported today, including a 6.4% rate of AMR¹ compared to an expected 30% rate of AMR² in this highly sensitized population of kidney transplant recipients. The data were presented today in an oral presentation at the 2013 annual congress of the European Society for Organ Transplantation (ESOT) in Vienna, Austria.

Acute AMR can lead to severe kidney allograft damage resulting in rapid loss of function and possible loss of the transplanted kidney, which makes AMR a significant clinical barrier to transplantation in sensitized patients.³ Research suggests that uncontrolled activation of complement, triggered by the binding of donor-specific antibodies (DSAs) to their target proteins (antigens) of the donor kidney, may be the primary reason for acute AMR in kidney transplant recipients who are sensitized, or have DSAs, to their donors.^{3,4} Prophylaxis with a terminal complement inhibitor, such as eculizumab, is thus considered a potential strategy to prevent acute AMR. There are no approved treatments for the prevention of acute AMR.

"Approximately 30% of kidney transplant candidates on waiting lists are sensitized, or have antibodies, to potential donors. Because conventional immunosuppressive therapies are ineffective for the prevention of AMR, sensitized patients often have to wait years for a kidney suitable for transplantation. Thus, AMR has emerged as a significant, long-standing clinical problem in transplantation," said Denis Glotz, M.D., Ph.D., Chief of the Department of Nephrology and Transplantation at Saint-Louis Hospital in Paris, France. "The data from this study suggest that eculizumab may be an effective prophylaxis against acute AMR in kidney recipients with preexisting antibodies against their donor."

"This study suggests that eculizumab, by inhibiting the activation of terminal complement, could be effective in preventing acute AMR, which is a severe and life-threatening complication in sensitized patients undergoing kidney transplantation," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "We are encouraged by the data presented today from this deceased-donor study, and also continue to enroll patients in our multi-national living-donor transplant trial in patients at elevated risk of AMR."

Eculizumab is approved in over 40 countries as a treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH) and in the United States, European Union and other countries for patients with atypical hemolytic uremic syndrome (aHUS). PNH and aHUS are both debilitating and life-threatening ultra-rare disorders caused by chronic, uncontrolled complement activation. Eculizumab is not approved for the prevention of AMR in any country and was used in the reported study on an investigational basis.

About the Study

Nine-week preliminary results were presented from an open-label, single-arm, multicenter Phase 2 trial in which 47 sensitized recipients of kidneys from deceased donors were treated with eculizumab. The mean age of the study participants was 50 years (range: 29-70).¹

The study's primary efficacy composite endpoint was post-transplantation treatment failure rate at Week 9, defined by biopsy-proven AMR, graft loss, patient death, and/or loss to follow-up. Preliminary results presented today are for the primary endpoint modified with utilization of local laboratory data (the pre-specified primary endpoint uses central lab data). At Week 9, 5 patients (10.6%; 95% confidence interval [CI]: 3.5%, 23.1%) were considered treatment failures, of which 3 (6.4%) had acute AMR. The three most common serious adverse events from Weeks 1 to 11 were complications of the transplanted kidney (12.8%), transplant rejection (8.5%), and acute renal failure (8.5%). One patient (2%) in the study died due to a post-operative myocardial infarction deemed not related to eculizumab.¹

About Acute Antibody-Mediated Rejection (AMR)

Acute antibody-mediated rejection (AMR) is a severe and potentially life-threatening condition that can lead to severe kidney allograft damage resulting in rapid loss of function and possible loss of the transplanted kidney. Patients who are sensitized (have high levels of donor-specific antibodies or DSAs) are at high risk for developing acute AMR, may have difficulty finding a viable donor organ, and therefore may never become eligible for transplantation. The development of acute AMR is believed to be primarily a result of uncontrolled complement activation caused by DSAs, which in turn frequently results in allograft damage and dysfunction, potential graft loss, and/or shortened graft survival.

While solid organ transplantation is the most effective form of therapy for the treatment of patients with end-stage renal disease (ESRD),⁵ concern about the consequences of AMR remains a significant obstacle to transplantation, as it results in significant delays for affected patients to access a suitable transplant. Overall, ESRD patients on dialysis have a very high mortality rate since approximately 65% of these patients die within 5 years of commencing dialysis.⁶ Additionally, approximately one-third of patients on the kidney transplant waiting list are sensitized to their potential donors⁷ and historically, approximately 30% of this highly sensitized population has developed AMR.² A therapy that prevents acute AMR is critically important

for sensitized patients with ESRD. Currently, there are no approved therapies for the prevention of acute AMR.

About Soliris

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 United States (US), European Union (EU) and other countries as the first and only treatment for aHUS patients. Soliris is indicated to inhibit complement-mediated TMA. Soliris is not indicated for the treatment of patients with Shiga toxin E. coli-related hemolytic uremic syndrome (STEC-HUS). Alexion is evaluating the safety and efficacy of Soliris for the treatment of patients with STEC-HUS.

Soliris also is approved in the US, EU, Japan 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.

Alexion's breakthrough approach in terminal complement inhibition has received 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, including the full prescribing information on Soliris, is available at www.soliris.net.

Important Safety Information

The US 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. 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 Serious Meningococcal Infections (5.1) for additional guidance on the management 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. 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 hypertension, upper respiratory tract infection, diarrhea, headache, anemia, vomiting, nausea, urinary tract infection, and leukopenia. Please see full prescribing information for Soliris, including boxed WARNING regarding risk of serious meningococcal infection.

About Alexion

Alexion Pharmaceuticals, Inc. is a biopharmaceutical company focused on serving patients with severe and ultra-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 PNH and aHUS, two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is currently approved in more than 40 countries for the treatment of PNH, and in the United States and European Union for the treatment of aHUS. Alexion is evaluating other potential indications for Soliris and is developing four other highly innovative biotechnology product candidates, which are being investigated across additional severe and ultra-rare disorders beyond PNH and aHUS. 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, regulatory and commercial milestones and potential health and medical benefits of Soliris® (eculizumab) for the prevention of antibody mediated rejection (AMR) in kidney transplant recipients. 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 June 30, 2013 and in our other filings with the US 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.

¹ 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.

² 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.

³ 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.

⁴ 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.

⁵ Russell JD, Beecroft ML, Ludwin D, Churchill DN. The quality of life in renal transplantation—a prospective study. *Transplantation* 1992;54(4):656-60.

⁶ Kidney disease statistics for the United States. US Department of Health & Human Services, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). NIH Publication No. 12—3895; 2012.

⁷ About CPRA for Professionals. US Department of Health & Human Services, Organ Procurement and Transplantation Network.
<http://optn.transplant.hrsa.gov/resources/allocationcalculators.asp?index=77>. Accessed September 9, 2013.

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