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Alexion Initiates Multinational Registration Trial of Eculizumab for the Prevention of Delayed Graft Function (DGF) after Kidney Transplantation

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced the initiation of dosing in a single, multinational, placebo-controlled clinical trial to evaluate the efficacy and safety of eculizumab (Soliris[®]) for the prevention of delayed graft function (DGF) after kidney transplantation in adult patients who are at increased risk of DGF. DGF is an early and serious complication of organ transplantation that affects approximately 25 percent,¹ and possibly up to 50 percent,² of deceased-donor kidney transplant cases, and is characterized by the failure of a transplanted organ to function normally immediately following transplantation. Patients experiencing DGF after a kidney transplant require dialysis in order to survive.³⁻⁵

Worldwide, there is an unmet medical need for a highly innovative therapy for patients at high risk of developing DGF, as there are no approved treatments to prevent DGF after kidney transplantation.⁶ In most cases DGF results from ischemia/reperfusion injury (IRI). IRI is due to multiple processes that occur following the restoration of blood flow to an area that had previously experienced deficient blood flow.⁷ Uncontrolled complement activation following IRI is believed to play a major role in the development of DGF.⁸⁻¹¹

"Delayed graft function is a serious and significant complication to successful kidney transplantation, which can be life-threatening due to the risk of losing the transplanted organ," said Martin Mackay, Ph.D., executive vice president and global head of R&D at Alexion. "Since complement activation plays a critical role in the development of DGF, a terminal complement inhibitor like eculizumab may have the potential to prevent this devastating complication. In addition, as donor organs are in short supply, reducing the risk of DGF may allow more deceased-donor organs to be successfully transplanted, which could potentially shorten the waiting time to receive a transplant."

Soliris is currently approved in nearly 50 countries for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) and in nearly 40 countries for the treatment of atypical hemolytic uremic syndrome (aHUS), two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is not approved in any country for the prevention of DGF after kidney transplantation.

About the DGF Study

The trial is a multinational, double-blind, placebo-controlled study with the primary objective of assessing the efficacy and safety of a two-dose regimen of eculizumab to prevent DGF in adult recipients of deceased-donor kidney transplants who are at increased risk of DGF. The primary endpoint is the incidence of DGF, defined as the requirement for dialysis for any reason in the first seven days post-treatment. Secondary endpoints include safety and tolerability as well as additional efficacy outcome measures. Patient enrollment and dosing have commenced in this trial. Recruitment is open to adults with dialysis-dependent renal failure who are to receive a first kidney transplant from a deceased donor at high-risk of developing DGF.² More information about the trial is available at www.clinicaltrials.gov under the identifier NCT02145182.

In January 2014 the U.S. Food and Drug Administration (FDA) granted eculizumab an orphan drug designation for the prevention of DGF in renal transplant patients. Eculizumab was also granted orphan medicinal product designation from the European Commission for the prevention of DGF after solid organ transplantation in February 2014.

About Delayed Graft Function (DGF)

DGF is an early and serious complication of organ transplantation that is characterized by the failure of a transplanted organ to function immediately following transplantation. When DGF occurs in the setting of kidney transplantation, the patient requires dialysis after the transplantation procedure.³⁻⁵ Most often, DGF results from organ injury caused by severe inflammation and complement activation associated with the normal processes of removal and transplantation of the donor organ.^{3-5,12} 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.^{13,14} In addition, as donor organs are in short supply, reducing the risk of DGF for organs that are at higher risk of developing 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,^{15,16} denying many patients the benefit of transplantation.

Currently, there are no approved therapies to prevent DGF after kidney transplantation.

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), 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. 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). 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). For the breakthrough innovation in complement inhibition, Alexion and Soliris have 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 U.S. prescribing information on Soliris is available at:
http://soliris.net/sites/default/files/assets/soliris_pi.pdf.

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 PNH and 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.alexionpharma.com.

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Safe Harbor Statement

This news release contains forward-looking statements, including statements related to potential medical benefits of Soliris® (eculizumab) for the prevention of delayed graft function (DGF) after kidney transplantation. 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 prevention of DGF after

kidney transplantation, delays in arranging satisfactory manufacturing capabilities, the possibility that results of clinical trials are not predictive of safety and efficacy results of Soliris for prevention of DGF in broader or different patient populations, decisions of regulatory authorities to require additional testing, the risk that estimates regarding the number of patients at risk of DGF and observations regarding the natural history of patients with DGF 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 Annual Report on Form 10-K for the period ended June 30, 2014. 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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