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Alexion Announces Top-Line Results from Phase 2/3 PROTECT Study of Eculizumab (Soliris®) for the Prevention of Delayed Graft Function (DGF) After Kidney Transplantation

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ: ALXN) today reported results from the PROTECT Study, a Phase 2/3 registration trial of eculizumab (Soliris®) for the prevention of delayed graft function (DGF) after kidney transplantation in adult recipients of a deceased donor kidney. The primary endpoint of incidence of DGF with a two-dose regimen of eculizumab compared with placebo did not reach statistical significance. DGF is an early and serious complication of organ transplantation in which the transplanted organ fails to function normally immediately following transplantation, and was defined in the study as the requirement for dialysis for any reason in the first 7 days post-transplant.[1,2] The primary endpoint also included incidence of death, graft loss, and loss to follow-up, including discontinuation.

"We are disappointed that this trial did not meet its primary endpoint, given the urgent need for preventive therapies for patients at risk of DGF and the potential role of the complement cascade in the development of this serious and life-threatening complication," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "We continue to analyze the data to better understand what the findings mean for patients undergoing a kidney transplant. Importantly, the safety of eculizumab in this trial appears consistent with the favorable safety profile observed in nearly a decade of real-world experience with this highly innovative therapy."

The PROTECT Study is a randomized, parallel-group, double-blind, placebo-controlled, multi-center study of eculizumab administered in an acute setting for the prevention of DGF in adult recipients of a deceased-donor kidney transplant who are at increased risk of DGF. A total of 288 patients were treated across North America, South America, Europe, and Australia. Patients had dialysis-dependent renal failure (initiated more than 2 months prior to transplant) and were scheduled to receive a first kidney transplant from a deceased standard criteria donor (SCD) or expanded criteria donor (ECD) with a DGF risk score of ≥25 percent using the Irish scale.

Patients were randomized 1:1 to receive either eculizumab or placebo in the following dosing regimen: one dose of eculizumab 1200 mg or placebo just prior to the time of reperfusion of the kidney allograft and one dose of eculizumab 900 mg or placebo within 18 to 24 hours of the completion of administration of the first dose. Randomization was stratified according to whether the donor kidney was preserved by cold storage or by machine perfusion, as well as by donor type (ECD vs. SCD). Patients were evaluated over a primary study period through 26 weeks and a follow-up period through 52 weeks.

In the primary endpoint of the study, assessed in 286 patients who were treated and received a transplant, the incidence of DGF, death, graft loss, or loss to follow-up at 7 days post-transplant was 35.9 percent for patients receiving a two-dose regimen of eculizumab compared with 41.7 percent for patients receiving placebo (p=0.398). In the first 60 days following treatment, rates of serious adverse events were higher for patients in the placebo group compared with the eculizumab group (54.1 percent vs. 44.4 percent). There were 4 deaths in the placebo group vs. 1 in the eculizumab group in the same time frame. Alexion expects that data from the study will be published at a later date.

Eculizumab received orphan drug designation (ODD) in 2014 from the U.S. Food and Drug Administration for the prevention of DGF in renal transplant patients, and from the European Medicines Agency for the prevention of DGF after solid organ transplantation. Soliris (eculizumab) is not approved in any country for the treatment or prevention of DGF.

About Delayed Graft Function

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.[1,2] When DGF occurs in the setting of kidney transplantation, the patient requires dialysis after the transplant procedure.[3-5] 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.[3-6] 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.[7,8] 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 to 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, denying many patients the benefit of transplantation.[9,10]

Currently, there are no approved therapies to prevent or treat 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) 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.

About Alexion

Alexion is a global biopharmaceutical company focused on developing and delivering life-transforming therapies for patients with devastating and rare disorders. Alexion is the global leader in complement inhibition and has developed and commercializes 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. In addition, Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). 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 Alexion's development plans for eculizumab (Soliris®) for the treatment of delayed graft function, the potential medical benefits of Soliris for the treatment of delayed graft function, and Alexion's future clinical, regulatory and commercial plans for Soliris for the treatment of delayed graft function. 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 our products, delays, interruptions or failures in the manufacture and supply of our products and our product candidates, progress in establishing and developing commercial infrastructure, failure to satisfactorily address matters raised by the FDA and other regulatory agencies, the possibility that results of clinical trials are not predictive of safety and efficacy results of our products in broader patient populations in the disease studied or other diseases, the risk that strategic transactions will not result in short-term or long-term benefits, the possibility that clinical trials of our product candidates could be delayed or that additional research and testing is required by regulatory agencies, the adequacy of our pharmacovigilance and drug safety reporting processes, the risk that third party payors (including governmental agencies) will not reimburse or continue to reimburse for the use of our products at acceptable rates or at all, risks regarding government investigations, including investigations of Alexion by the SEC and DOJ, risks relating to the internal investigation being conducted by the Audit and Finance Committee, the risk that estimates regarding the number of patients with the diseases that our products treat are inaccurate, the risks of shifting foreign exchange rates, and a variety of other risks set forth from time to time in Alexion's filings with the U.S. 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, 2016 and in our other filings with the U.S. 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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