Early Clinical Experience and Basic Science Support Further Investigation of Soliris(R) (eculizumab) for the Treatment of Patients with Thrombotic Microangiopathy

Case Reports and Basic Science Presented at International Conference on HUS, PNH and MPGN

CHESHIRE, Conn., Jun 15, 2010 (BUSINESS WIRE) -- Researchers reported today that Soliris$^{(R)}$ (eculizumab), a first-in-class terminal complement inhibitor developed by Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN), may provide clinical benefits to patients with thrombotic microangiopathy (TMA) resulting from uncontrolled complement activation. TMA, the formation of blood clots in capillaries and small arteries, can lead to life-threatening damage in multiple organs including kidney failure, thrombocytopenia (abnormally low platelet count) and anemia.

TMA is common among patients with certain ultra-rare, severe complement inhibitor deficiency diseases, including atypical Hemolytic Uremic Syndrome (aHUS), Membranoproliferative Glomerulonephritis (MPGN), Catastrophic Antiphospholipid Syndrome (CAPS) and Paroxysmal Nocturnal Hemoglobinuria (PNH). Research examining the role of Soliris in these disorders was the subject of 10 presentations at the 2nd International Conference on HUS-MPGN-PNH held in Innsbruck, Austria on June 13-15, 2010.

"aHUS, MPGN, CAPS and PNH are diseases characterized by uncontrolled complement activation that share a common pathology of TMA. Research shows that these defects in the body's complement system often result in devastating and life-threatening clinical consequences," said Dr. Lothar Bernd Zimmerhackl, President of the Conference and Professor at the Medical University of Innsbruck. "As we gain more clinical experience and learn more about these diseases, terminal complement inhibition with eculizumab is a promising treatment strategy, since it targets a central mechanism of TMA."

Soliris has been approved by healthcare authorities in the United States, European Union, Japan and other countries as the first treatment for patients with PNH, a rare, debilitating and life-threatening blood disorder defined by hemolysis, or the destruction of red blood cells. Soliris is not approved for the treatment of aHUS, MPGN, CAPS or diarrhea-associated HUS (D+HUS).

"Research presented this week in Innsbruck suggests that Soliris has the potential to benefit patients with a variety of ultra-rare genetic diseases characterized by the presence of TMA," said Leonard Bell, M.D., Chief Executive Officer of Alexion. "Our primary focus is to diligently bring Soliris to patients with PNH in a growing number of countries worldwide. We recognize the often devastating outcomes for patients who have very few and limited therapeutic options, and we are committed to evaluating the safety and efficacy of Soliris in these diseases where we believe complement inhibition could have a dramatic impact on patients' lives."

Early Clinical Experience with Soliris in Atypical HUS
Researchers reported several case studies of patients with atypical Hemolytic Uremic Syndrome (aHUS) treated with Soliris. As previously announced, Alexion has completed enrollment in four prospective, open-label clinical studies investigating Soliris as a potential treatment for patients with aHUS, and preliminary results from these studies are expected later this year. Presentations at the conference included:

- **"Eculizumab in Atypical Hemolytic Uremic Syndrome: Long-Term Clinical Course and Histological Findings," S. Tschumi.**
  A nine year-old girl with aHUS requiring plasma exchange was switched to treatment with Soliris (600 mg every two weeks). Nine months after starting Soliris, kidney function remained stable, anti-hypertensive medications were reduced, cardiac thickening was reduced, and quality of life was substantially improved. A renal biopsy performed at two months after starting Soliris showed that there was no evidence of TMA.

- **"Remission of Plasma-Resistant Atypical Hemolytic Uremic Syndrome Relapse on Kidney Graft with Eculizumab," G. Ardissino.**
  A six year-old boy with aHUS received a kidney transplant. Two months after the transplant, aHUS exacerbated without any apparent antecedent precipitant resulting in kidney failure requiring dialysis, despite plasma exchange. Soliris treatment was commenced and was associated with improvement in kidney function allowing cessation of dialysis. Investigators noted that Soliris appeared safe in this individual.

- **"Maintenance of Renal Function Under Eculizumab Despite Discontinuation of Plasma Exchange After a Third Transplantation for Atypical Hemolytic Uremic Syndrome Associated with a CFH Mutation," J.C. Davin.**

A 17-year old patient with aHUS and history of multiple severe brain ischemic events underwent a third kidney transplant and was started on plasma exchange therapy. The patient experienced repetitive aHUS exacerbations and also became severely intolerant of plasma with severe allergic reactions. The patient was started on Soliris treatment at the dose of 1200 mg every two weeks and plasma exchange was discontinued. The patient tolerated Soliris well during fifteen months of treatment. During this ongoing treatment her plasma creatinine was stable, and neither aHUS exacerbation nor side-effects have been observed.

- **"Effectiveness of Eculizumab in a Plasma Infusion Dependent Patient with Atypical Hemolytic Uremic Syndrome Associated with Heterozygous Combined De Novo Mutations in Factor H Gene," A.L. Lapeyraque.**
A seven year-old girl with aHUS had been treated prophylactically with plasma infusions and with increased plasma infusion frequency after exacerbations. After plasma infusions were determined to be ineffective, the patient was started on Soliris treatment. The patient experienced immediate and complete inhibition of terminal complement activation. Already during the first week of treatment, her platelet count increased, hemolysis and blood pressure normalized and renal function recovered. The patient is chronically treated with 600 mg of Soliris every two weeks for over six months with no evidence of platelet consumption or hemolysis.

- **"Successful Kidney Transplantation in Four Patients With Factor H Deficiency-HUS," G. Ardissino.**
Four patients with Factor H deficiency HUS (FHD-HUS) had kidney transplants following one plasma exchange before transplant and prophylactic plasma exchanges and plasma infusion after transplant. Two out of the four patients experienced aHUS recurrence despite prophylactic plasma therapy. One patient was managed with Soliris and was reported to have achieved immediate recovery from the recurrence.

Rationale for Terminal Complement Inhibition in Patients with MPGN
MPGN is a rare and progressive renal disease that is typically found in children and young adults. There are two types of MPGN: MPGN type I and MPGN type II which is also known as Dense Deposit Disease (DDD). In both types, a dysregulation in the alternative pathway of the complement system is considered to play a role in the pathogenesis. Presentations included:

- **"Treatment of a Patient with Dense Deposit Disease with Eculizumab (Soliris)," M. Vivarelli, F. Emma.**
Results were reported on a 17-year-old patient who was diagnosed with DDD with normal renal function but significant proteinuria (3-5 grams/24 hrs). To date, the patient has been treated with Soliris for 16 months. The reported results indicate that Soliris treatment was associated with a significant increase in serum protein and albumin, as well as a decrease in both the urine protein/creatinine ratio and 24 hour protein. His creatinine and blood pressure remain normal. The investigators reported no drug-related adverse effects while on Soliris over the 16-month treatment period and concluded that Soliris may be an important therapeutic option for patients with DDD.

- **"Membrano Proliferative Glomerulonephritis: 3 Case Reports," S. Hartl.**
Researchers report on three patients with MPGN, two with MPGN type I and one with MPGN type II or DDD, with different clinical courses and biopsy results. The activation of the complement system and antibodies against the C3 convertase play an important role in all three patients. The researchers suggest that the C5 convertase might be a sophisticated target in MPGN and a clinical trial with the anti-C5 antibody Soliris might be an important step in advancing the treatment in this severe disease. An international registry has been set-up to be the basis for further clinical trials using Soliris in patients with MPGN.

- **"A Novel Disease Mechanism for MPGN II/DDD: Increased CFHR1 Expression Results in Competitive Loss of CFH Cofactor Activity," C. Licht.**
Researchers present a case of an 11 year-old boy with DDD who, despite treatment, progressed to end stage kidney disease within months and was started on peritoneal dialysis. After four years, he received a transplant but developed disease recurrence within one week. Plasma therapy was transiently successful, but after nine months the treatment effect was lost and renal function again severely deteriorated resulting in severe and uncontrollable hypertension requiring kidney removal. A genetic analysis identified 3 copies of CFHR1. The researchers identified that a surplus of CFHR1 could play a role in disease recurrence early post treatment, and that more efficient treatment strategies like targeted complement blockade are required for patients with DDD.

Other Clinical Experience with Soliris in TMA Diseases: PNH, CAPS and D+HUS
Several encouraging case studies were reported and provide further insight into the potential benefits of Soliris in treating patients with other TMA-related diseases, including PNH, CAPS, and D+HUS.

- **"Current Experience with Eculizumab and Future Aspects," M. Riedl on behalf of L.B. Zimmerhackl.**
The report from Dr. Zimmerhackl's group highlighted a recent publication in the New England Journal of Medicine (1) that described the investigational use of Soliris to achieve the first reported successful kidney transplant for a patient suffering from CAPS, another ultra rare life-threatening disease characterized by multi-organ failure as a consequence of TMA.
- **"Eculizumab in Diarrhea-Associated Hemolytic Uremic Syndrome," C. Mache.**
A 28 year-old patient with positive serology for *E. coli* 0157, acute renal failure with hemolysis and platelet consumption,

decreased early complement protein levels, and no identifiable complement mutation was treated with hemodialysis, steroids and frequent plasma exchange. With no improvement and continued dialysis requirement during 30 days of this treatment, Soliris treatment was commenced. The patient's platelet count was normalized after 29 days, serum haptoglobin levels after 85 days, and serum LDH after 99 days. In addition, renal function had improved permitting termination of hemodialysis after 22 days. At the time of this conference (five months post initiation of therapy), Soliris is still sustaining suppression of TMA, and maintaining renal function with a serum creatinine of 2.3 mg/dL.

- **"Rescue Therapy with Eculizumab Fails to Prevent Graft Loss in a Renal Transplant Patient with Factor I Mutation: Chronic Rejection or Recurrence?" S. Loos.**
  A patient with D-HUS (presumably aHUS), who had already had 2 failed kidney transplants, each with evidence of aHUS-associated TMA on kidney biopsy, was transplanted a third time with chronic plasma therapy in 2008. In 2009, the patient progressed to kidney failure despite intravenous steroids and addition of further immunosuppressive medications. At that time, the kidney biopsy showed interstitial fibrosis without biopsy evidence of TMA or humoral rejection in the kidney. The kidney allograft function had already declined significantly, and treatment with Soliris was commenced. This case highlights the problem of defining HUS recurrence in failing renal transplant.

About PNH

PNH is a rare blood disorder that strikes people of all ages, with an average age of onset in the early 30s. (2) Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger. (3) PNH develops without warning and can occur in men and women of all races, backgrounds and ages. PNH often goes unrecognized, with delays in diagnosis ranging from one to more than 10 years. (4) It is estimated that approximately one-third of patients with PNH do not survive more than five years from the time of diagnosis. (4) PNH has been identified more commonly among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndromes (MDS). (5,6, 7) In patients with thrombosis of unknown origin, PNH may be an underlying cause. (2) More information on PNH is available at www.pnhsource.com.

About aHUS

Atypical hemolytic-uremic syndrome (aHUS) is an ultra-rare, chronic and progressive genetic disorder characterized by sudden clinical deterioration - life-threatening blood clots throughout the body leading to renal failure, thrombocytopenia, and hemolytic anemia. These clinical abnormalities are the hallmark of thrombotic microangiopathy.

Patients with aHUS experience poor outcomes. Approximately 60 percent of patients with the most common mutation experience renal failure, dialysis, or death within one year of the first clinical episode. (9, 10) Following kidney transplantation, recurrent aHUS causes kidney failure in up to 60 to 90 percent of patients. (11) As in PNH, aHUS is caused by a deficiency in normally occurring complement inhibitor proteins. Typically, patients with aHUS have genetic mutations in one of several complement inhibitor proteins that lead to uncontrolled complement activation. Excessive complement activation is associated with severe inflammation of the blood vessels and blood clotting through the activation of white blood cells, platelets, and the endothelial cell lining of blood vessels. (8)

About Soliris

Soliris (eculizumab) is a first-in-class terminal complement inhibitor developed from the laboratory through regulatory approval by Alexion. Soliris has been approved by the healthcare authorities in the U.S., European Union, Japan and other countries as the first treatment for patients with PNH, a rare, debilitating and life-threatening blood disorder defined by hemolysis, or the destruction of red blood cells. Prior to these approvals, there was no therapy specifically available for the treatment of PNH. Soliris is not approved for treatment of atypical Hemolytic Uremic Syndrome (aHUS), Membranoproliferative Glomerulonephritis (MPGN), Catastrophic Antiphospholipid Syndrome (CAPS) or diarrhea-associated HUS (D+HUS).

Patients with PNH in more than 20 countries now have access to Soliris therapy through national or private healthcare providers. As the first terminal complement inhibitor to be approved in countries around the world, Soliris represents a long-sought breakthrough in medical innovation. Alexion's innovative approach to complement inhibition has received some of 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 on Soliris is available at www.soliris.net.

Important Safety Information

Soliris is generally well tolerated in patients with PNH. The most frequent adverse events observed in clinical studies of patients with PNH were headache, nasopharyngitis (runny nose), back pain and nausea. Treatment with Soliris should not alter anticoagulant management because the effect of withdrawal of anticoagulant therapy during Soliris treatment has not been established.

The U.S. product label for Soliris also includes a boxed warning: "Soliris increases the risk of meningococcal infections.

Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Vaccinate patients with a meningococcal vaccine at least two weeks prior to receiving the first dose of Soliris; revaccinate according to current medical guidelines for vaccine use. Monitor patients for early signs of meningococcal infections, evaluate immediately if infection is suspected, and treat with antibiotics if necessary." During PNH clinical studies, two out of 196 vaccinated PNH patients treated with Soliris experienced a serious meningococcal infection. Prior to beginning Soliris therapy, all patients and their prescribing physicians are encouraged to enroll in the PNH Registry, which is part of a special risk-management program that involves initial and continuing education and long-term monitoring for detection of new safety findings.

About Alexion

Alexion Pharmaceuticals, Inc. is a biopharmaceutical company working to develop and deliver life-changing drug therapies for patients with serious and life-threatening medical conditions. Alexion is engaged in the discovery, development and commercialization of therapeutic products aimed at treating patients with a wide array of severe disease states, including hematologic and kidney diseases, transplant, other inflammatory disorders, and cancer. Soliris is Alexion's first marketed product. Alexion is evaluating other potential indications for Soliris as well as other formulations of eculizumab for additional clinical indications, and is pursuing development of other antibody product candidates in early stages of development. 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 milestones and potential health and medical benefits of Soliris (eculizumab) for the treatment of patients with Paroxysmal Nocturnal Hemoglobinuria, and the potential treatment of patients with atypical Hemolytic Uremic Syndrome (aHUS), Membranoproliferative Glomerulonephritis (MPGN), Catastrophic Antiphospholipid Syndrome (CAPS) or diarrhea-associated HUS (D+HUS). 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, delays in arranging satisfactory manufacturing capability and establishing commercial infrastructure, the possibility that results of published reports or clinical trials are not predictive of safety and efficacy results of Soliris in broader patient populations, the risk that clinical trials may not be completed successfully, the possibility that initial results of commercialization are not predictive of future rates of adoption of Soliris, the risk that third parties won't agree to license any necessary intellectual property to Alexion on reasonable terms or at all, the risk that third party payors will not reimburse for the use of Soliris at acceptable rates or at all, 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, 2010, and in Alexion's other filings with the 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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SOURCE: Alexion Pharmaceuticals, Inc.

Alexion Pharmaceuticals, Inc.
Irving Adler, 203-271-8210
Sr. Director, Corporate Communications
or
Media:
Makovsky & Company
Mark Marmur, 212-508-9670
or
Investors:
Rx Communications
Rhonda Chiger, 917-322-2569