Longer-Term Data on Soliris Showed Significant and Sustained Benefits for Patients with aHUS

Data from Phase 2 Soliris Extension Studies Presented at ASN Meeting

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) today presented longer-term data from the extensions of two pivotal phase 2 studies of Soliris® (eculizumab) in patients with atypical hemolytic uremic syndrome (aHUS): (i) a study in patients with a long duration of disease prior to receiving intervention with Soliris following chronic plasma exchange/infusion (PE/PI) and (ii) a study in patients with a shorter duration of disease prior to intervention with Soliris who had progressive clinical complications despite intensive PE/PI. Results demonstrated that ongoing treatment with Soliris sustained the suppression of complement-mediated thrombotic microangiopathy (TMA), maintained or further improved longer-term renal function, and enhanced quality of life. These data were presented at the annual meeting of the American Society of Nephrology (ASN) in Philadelphia.

aHUS is an ultra-rare, life-threatening, chronic genetic disease that can progressively damage vital organs, leading to stroke, heart attack, kidney failure and death.[1] The morbidity and premature mortality in aHUS is caused by chronic uncontrolled activation of the complement system, resulting in TMA, the formation of multiple blood clots in small blood vessels throughout the body.[2,3] Soliris, a first-in-class terminal complement inhibitor, specifically targets uncontrolled complement activation, inhibiting complement-mediated TMA and its severe clinical consequences.

On September 23rd, the U.S. Food and Drug Administration (FDA) granted accelerated approval of Soliris for the treatment of pediatric and adult patients with aHUS to inhibit complement-mediated TMA. The effectiveness of Soliris in aHUS is based on the effects on TMA and renal function. Prospective clinical trials in additional patients are ongoing to confirm the benefit of Soliris in patients with aHUS. Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS). Also on September 23rd, the European Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending that the therapeutic indication for Soliris be extended to include the treatment of pediatric and adult patients with aHUS in Europe.

"Data presented today support that early and ongoing treatment with the complement inhibitor Soliris is beneficial for patients with aHUS," said Leonard Bell, M.D., Chief Executive Officer of Alexion. "In these extension studies, continued treatment with Soliris sustained suppression of complement-mediated TMA, which resulted in further improvement in kidney function and continued improvement in quality of life for these patients with aHUS."

Patients with a Longer Duration of Disease Prior to Soliris Therapy (Previously Receiving Chronic PE/PI)

In a poster session today, researchers presented longer-term findings from a prospective, open-label, single-arm phase 2 trial of Soliris in adult and adolescent patients with a long duration of aHUS and prior treatment before starting on Soliris. Patients had been diagnosed with aHUS a median of 48 months prior to starting the study, and nearly all (90%) had chronic renal insufficiency at baseline (eGFR < 60 mL/min/1.73 m2). In the study, 20 patients received Soliris through week 26, and 19 patients continued into a long-term extension study and were evaluated at 62 weeks median duration of Soliris treatment (range of 26-74 weeks).

The primary endpoint of TMA event-free status (at least 12 consecutive weeks of stable platelet count, no PE/PI, and no new dialysis) was achieved by 16 of 20 Soliris-treated patients (80%) by week 26 and was sustained through the extension study, indicating that chronic treatment with Soliris continued to significantly inhibit complement-mediated TMA and progression of kidney dysfunction. Hematologic normalization was achieved in 18 of 20 Soliris-treated patients (90%) and was sustained through data cut-off. Importantly, PE/PI was eliminated in 100% of patients and no patients required new dialysis through week 26 and through data cut-off.

Ongoing Soliris treatment was associated with a highly significant and continuous, time-dependent improvement in eGFR (6 mL/min/1.73m^2 [95%CI: 3, 9]) through week 26 and throughout the extension study ($p<0.0001$). Nine out of 20 patients (45%) also improved ≥1 chronic kidney disease (CKD) stage from baseline through data cut-off. Notably, earlier intervention with Soliris was associated with an increased likelihood of improved kidney function, as measured by eGFR, at week 26 ($p=0.04$). In addition, 73% of patients achieved a clinically meaningful benefit in health-related quality of life through week 26, and maintained this benefit with longer-term treatment.

"This study in patients with a long duration of disease and substantial renal damage prior to starting on Soliris, showed that continued treatment with Soliris led to sustained suppression of TMA, stabilized or even improved kidney function, and permanent discontinuation of plasma exchange or infusion," said Christoph Licht, M.D., FASN, Associate Professor of Paediatrics Division of Nephrology at the Hospital for Sick Children, University of Toronto[4]. "These longer-term data strengthen the evidence that chronic treatment with Soliris has the potential to transform the clinical course of aHUS."

Soliris was well tolerated in the study. The most common drug-related adverse events (AEs) were headache, leukopenia and lymphopenia.

Patients with Shorter Duration of Disease Prior to Soliris Therapy and Progressive TMA Complications Despite Intensive PE/PI

In another poster session today, researchers presented longer-term data from a prospective, open-label, single-arm phase 2 study in adult and adolescent patients with progressive clinical TMA complications despite intensive PE/PI. Patients had been diagnosed with aHUS a median of 10 months before the start of the study, and 71% had severe renal impairment (eGFR <30 mL/min/1.73m^2) at baseline. Seventeen patients were enrolled in the study and 15 were treated with Soliris for 26 weeks. Thirteen patients continued into the long-term extension study and were evaluated at 64 weeks median duration of Soliris treatment (range of 2-90 weeks).

In the primary endpoint, mean platelet count increased 73x10^9/L (P=0.0001) from baseline through week 26 and was sustained through the extension study, indicating ongoing inhibition of complement-mediated TMA. All patients (100%) with low platelets at baseline who continued on chronic Soliris treatment through week 26 achieved platelet normalization, and all 13 patients who entered the extension study and continued on treatment maintained normal platelet levels. TMA event-free status was achieved in 15 of 17 Soliris-treated patients (88%) through week 26, and all 13 patients (100%) who entered the extension study sustained their TMA event-free status through each data cut-off point. Hematologic normalization was achieved in 13 of 17 Soliris-treated patients (76%), which was sustained through all data cut-off points. These results demonstrated that chronic treatment with Soliris inhibits complement-mediated TMA.

Researchers also observed that ongoing Soliris treatment was associated with a highly significant and continuous, time-dependent improvement in eGFR with a mean change from baseline of 31 mL/min/1.73m^2 through 26 weeks (p=0.0001) and one year (p=0.0005); in addition, four out of five (80%) patients eliminated dialysis with chronic Soliris treatment. Importantly, earlier initiation of Soliris treatment was associated with an increased likelihood of improved eGFR through week 26 (p=0.03). In addition, 80% of patients achieved a clinically meaningful change in health-related quality of life through week 26, increasing to 87% through the extension study.

"Sustained treatment with Soliris, particularly when initiated earlier, provided significant and persistent benefits for patients with aHUS in this study," said Larry Greenbaum, M.D., Ph.D., Director of Pediatric Nephrology at Emory University and Children's Healthcare of Atlanta[4]. "Soliris not only stabilized or improved kidney function, but also eliminated the need for dialysis. Every patient in this study had a reduction in complement activity, the underlying cause of TMA, with sustained Soliris therapy, which is an important outcome for a disease that previously led to progressive organ failure and shortened life span for patients."

Soliris was well tolerated in this study. The most common drug-related AEs were leukopenia, nausea, and vomiting.

About aHUS

aHUS is a chronic, ultra-rare, and life-threatening disease in which a genetic deficiency in one or more complement regulatory genes causes life-long uncontrolled complement activation, resulting in complement-mediated thrombotic microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body.[1,2] 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.[2,3] More than half of all patients with aHUS die, require kidney dialysis or have permanent kidney damage within 1 year of diagnosis.[5] The majority of patients with aHUS who receive a kidney transplant commonly experience subsequent systemic TMA, resulting in a 90% transplant failure rate.[6]

aHUS affects both children and adults. In a large group of aHUS patients, 60% were first diagnosed at younger than 18 years of age.[7] 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% of patients with a confirmed diagnosis of aHUS.[7]

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 US, European Union, 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 also approved in the US as the first and only treatment for patients with atypical Hemolytic Uremic Syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy, a debilitating, ultra-rare and life-threatening genetic disorder characterized by complement-mediated thrombotic microangiopathy (blood clots in small vessels). The effectiveness of Soliris in aHUS is based on the effects on thrombotic microangiopathy (TMA) and renal function. Prospective clinical trials in additional patients are ongoing to confirm the benefit of Soliris in patients with aHUS. Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS). Alexion's breakthrough approach in 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

Soliris is generally well tolerated in patients with PNH and aHUS. 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.

The U.S. product label for Soliris also 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 (5.2). Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-soliris (1-888-765-4747)."

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 35 countries for the treatment of PNH, and in the United States for the treatment of aHUS. Alexion is evaluating other potential indications for Soliris and is pursuing development of other innovative biotechnology 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, regulatory and commercial milestones and potential health and medical benefits of Soliris® (eculizumab) for the potential treatment of patients with 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 June 30, 2011, 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.

References and Footnotes

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4. Dr. Christoph Licht and Dr. Larry Greenbaum receive research support from Alexion Pharmaceuticals, Inc. and are consultants to the company.

5. Caprioli J, Noris M, Brioschi S, et al; for the International Registry of Recurrent and Familial HUS/TTP. Genetics of HUS: the impact of MCP, CFH, and IF mutations on clinical presentation, response to treatment, and outcome. Blood. 2006;108:1267-1279.

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