New Data Confirm Hemolysis as Predictor of Thromboembolism and Early Death in Patients with PNH and Demonstrate Need To Test High-Risk Patients for PNH

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) today announced the presentation of new data that underscore the severity of paroxysmal nocturnal hemoglobinuria (PNH), a debilitating, ultra-rare and life-threatening blood disorder. PNH is characterized by chronic, uncontrolled complement activation leading to hemolysis (red blood cell destruction), which is measured by the presence of higher than normal levels of lactate dehydrogenase (LDH) through routine laboratory testing. The new data include an analysis from the South Korean National Registry showing that hemolysis, as measured by LDH serum level at diagnosis, is a strong and independent predictor of severe complications, including early death in patients with PNH.[1] In another study, data confirmed the importance of screening high-risk patients for PNH to ensure that they are accurately diagnosed and can receive early intervention. These data were presented at the 53rd American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego.

"The research presented at ASH confirms the significant risks associated with hemolysis resulting from chronic uncontrolled complement activation, as well as the critical need for testing of patients at high-risk for PNH," said Leonard Bell, M.D., Chief Executive Officer of Alexion.

Chronic Uncontrolled Complement Activation and Resulting Hemolysis Is a Strong and Independent Predictor of Mortality

In a poster session today, researchers presented data from a retrospective analysis of 301 patients in the South Korean National Registry.[1] The analysis evaluated patient outcomes based on elevated LDH at diagnosis, a marker of uncontrolled complement activation.

Researchers found that patients whose LDH was at least 1.5 times the upper limit of normal (LDH≥1.5xULN) at diagnosis had a 4.8-fold greater mortality rate compared with the age- and gender-matched general population ($P < 0.001$). In contrast, patients with LDH < 1.5xULN at diagnosis had a similar mortality rate to the age- and gender-matched general population ($P=0.8245$). Moreover, researchers demonstrated that LDH ≥1.5x at diagnosis was a predictor of mortality independent of other factors, including age, gender, and bone marrow disorder [OR=10.57; 95% CI (1.36, 81.93); $P=0.024$].

The analysis also measured LDH levels at diagnosis of ≥ 3.0xULN and ≥ 5.0xULN in the studied patients and found that LDH ≥1.5xULN is a better predictor of thrombosis and mortality than these higher levels. Using an LDH threshold greater than 1.5xULN missed approximately 50% of the population that was at risk for life-threatening thromboses.

"This analysis shows that any PNH patient with elevated LDH is at risk for serious complications due to uncontrolled complement activation, reinforcing the need for early intervention in all patients," said lead investigator Jong Wook Lee, M.D., Ph.D., Professor of Medicine, Chair of the Division of Hematology, and Director of the Catholic Institute of Cell Therapy, Catholic Blood and Marrow Transplantation Center, Seoul St. Mary's Hospital, the Catholic University of Korea.[2] "Importantly, the study shows that LDH of 1.5 times the upper limit of normal is the correct clinical level for identifying patients likely to experience a thromboembolism or other life-threatening outcome, and that a higher threshold for LDH (3.0 and 5.0 x ULN) would omit evaluating significant numbers of patients at high risk for mortality."

Consistently Testing High-Risk Patients for PNH

In a poster session on Saturday, December 10, researchers presented an analysis of 6,897 patients who were screened for PNH clone blood cells using high-sensitivity flow cytometry (HSFC), the method for diagnosing PNH recommended by the International Clinical Cytometry Society (ICCS).[3] In the analysis, ICD-9 Diagnostic Codes were used to identify patients who had clinical indications for PNH testing in accordance with the ICCS guidelines. The analysis found that PNH clones (≥0.01%) were detected in 26% of patients with an ICD-9 diagnosis of aplastic anemia (AA), as well as in 23% of patients with hemolytic anemia, 19% of patients with hemoglobinuria and 8% of patients with hemolysis. In addition, among patients with bone marrow failure syndromes other than AA, 6% of patients with unexplained cytopenia, 6% of patients with myelodysplastic syndrome, and 4% of patients with anemia (unspecified or in chronic illness) tested positive for PNH.

"This study confirms the importance of consistently testing patients in high-risk populations for PNH based on the ICCS recommendations to ensure accurate diagnosis and early intervention," said study investigator Ilene Ceil Weitz, M.D., Associate Professor of Medicine, Jane Anne Nohl Division of Hematology, Keck School of Medicine of the University of Southern

California.[2] "The study also observed that changes in PNH clone size may occur over time, highlighting the need to monitor patients, particularly those with small initial PNH clones."

The study authors recommend annual monitoring of patients with PNH clone sizes < 0.1% and at least semi-annual monitoring for patients with PNH clone sizes > 0.1%.

Understanding Clinical Characteristics of PNH in Pediatric Patients

In a poster session on Sunday, December 11, researchers presented data from a large cohort of pediatric patients with PNH, as well as the first comparison of adult and pediatric patients.[4] The study compared data from 551 patients, classified into those diagnosed at less than 18 years of age (56 patients) and those diagnosed at age 18 or older (495 patients). Pediatric patients had substantial morbidity related to chronic uncontrolled complement activation and hemolysis with impaired renal function (13%), thrombosis (11%), fatigue (63%), abdominal pain (45%), dyspnea (41%), dysphagia (20%), and hemoglobinuria (66%). While adult rates of thrombosis and fatigue were higher than those observed in pediatric patients, the risk of thrombosis was much higher in pediatric patients with PNH compared with the general population. Incidence of thromboses in the general healthy pediatric population is as low as 0.0007%[5] compared with 10.7% observed in the medical history of pediatric patients diagnosed with PNH in this study, demonstrating that thrombosis remains a significant issue for all PNH patients, regardless of age.

In a separate poster session at ASH, researchers presented data from a 12-week, open-label multicenter study of Soliris® (eculizumab) in children and adolescents (ages 2 to 17 years) with PNH.[6] The study showed that Soliris treatment led to a rapid and sustained reduction in LDH levels, from a mean of 1,020 U/L at baseline to within normal range (275/U/L) by the second week of treatment. The safety and adverse event profile for Soliris was consistent with that reported in adult Phase 3 clinical trials.

About PNH

PNH is an ultra-rare blood disorder in which chronic, uncontrolled activation of complement, a component of the normal immune system, results in hemolysis (destruction of the patient's red blood cells). PNH strikes people of all ages, with an average age of onset in the early 30s.[7] Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger.[8] 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.[9] In the period of time before Soliris was available, it had been estimated that approximately one-third of patients with PNH did not survive more than five years from the time of diagnosis.[9] PNH has been identified more commonly among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndromes (MDS).[10,11,12] In patients with thrombosis of unknown origin, PNH may be an underlying cause.[7] More information on PNH is available at www.pnhsource.com.

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 and the European Union 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. 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). 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)."

Prior to beginning Soliris therapy, all patients and their prescribing physicians in the United States will be enrolled in the Soliris Safety 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.

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 and the European Union 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.

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 PNH and 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 September 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.

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References

(1) Abstract 3166, entitled "Uncontrolled Complement Activation and the Resulting Chronic Hemolysis As Measured by LDH Serum Level At Diagnosis As Predictor of Thrombotic Complications and Mortality in a Large Cohort of Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)," presented by Jong Wook Lee at the 53rd American Society of Hematology (ASH) Annual Meeting and Exposition, December 12, 2011.

(2) Dr. Jong Wook Lee and Dr. Ilene Ceil Weitz receive research support from Alexion Pharmaceuticals, Inc. and are consultants to the company.

(3) Abstract 1033, entitled "Incidence of PNH Clones by Diagnostic Code Utilizing High Sensitivity Flow Cytometry," presented by Mayur K. Movalia at the 53rd American Society of Hematology (ASH) Annual Meeting and Exposition, December 10, 2011.

(4) Abstract 2102, entitled "Clinical Characteristics of Classic Paroxysmal Nocturnal Hemoglobinuria (PNH) in Pediatric Patients: A Comparison with Classic PNH in Adults. An International PNH Registry Study," presented by Alvaro Urbano-Ispizua at the 53rd American Society of Hematology (ASH) Annual Meeting and Exposition, December 11, 2011.

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(6) Abstract 1034, entitled "Efficacy and Safety of Eculizumab in Children and Adolescents with Paroxysmal Nocturnal

Hemoglobinuria," presented by Ulrike M. Reiss at the 53rd American Society of Hematology (ASH) Annual Meeting and Exposition, December 10, 2011.

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