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Data from the International Paroxysmal Nocturnal Hemoglobinuria (PNH) Registry Presented at ASH Annual Meeting Underscore Devastating Nature of PNH and Benefits of Soliris® (eculizumab) Treatment

- Researchers Also Report Data from Long-Term Follow-up Study Supporting Effectiveness of Soliris in Preventing Thrombotic Microangiopathy (TMA) in Patients with Atypical Hemolytic Uremic Syndrome (aHUS) -

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ: ALXN) today announced that researchers presented data from the International Paroxysmal Nocturnal Hemoglobinuria (PNH) Registry that advance the understanding of PNH and provide important information for the medical community on the long-term management of the disease, including the progression of symptoms in untreated patients with PNH and the continued benefits of ongoing Soliris® (eculizumab) treatment regardless of transfusion history. Researchers also presented data from a long-term follow-up study evaluating the effectiveness of Soliris in preventing thrombotic microangiopathy (TMA) in patients with atypical hemolytic uremic syndrome (aHUS). Both PNH and aHUS are severe, ultra-rare diseases caused by chronic uncontrolled complement activation. These data were presented at the 57th Annual Meeting of the American Society of Hematology (ASH) in Orlando.

"Data from the International PNH registry, the most comprehensive source of long-term, real-world information on PNH, continue to reinforce the devastating nature of the disease and that without treatment, patients with PNH are at continuous risk for severe and devastating consequences resulting from the ongoing complement-mediated destruction of red blood cells. The registry data reinforce the strong clinical benefits to patients with PNH receiving ongoing treatment with Soliris," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "In addition, data from the long-term follow-up aHUS study underscore the clinical benefits to patients with aHUS receiving ongoing treatment with Soliris in reducing the rate and severity of TMA."

Data from the International PNH Registry

Three separate posters were presented at ASH from the International PNH Registry, a prospective, worldwide, observational study of patients with PNH that has enrolled more than 4,000 patients to date.

"The International PNH Registry provides key insights into the progressive, devastating and potentially irreversible consequences of PNH, as well as the long-term management of the disease," said Peter Hillmen, MB, ChB, PhD, Professor of Experimental Haematology, University of Leeds, and Honorary Consultant Haematologist at St James's University Hospital, Leeds, and Chair of the Executive Committee of the International PNH Registry. "Importantly, the data presented today indicate that transfusions are not the only indicator of the underlying disease process and burden in PNH, and that Soliris has a meaningful impact on hemolysis as measured by LDH levels, irrespective of a patient's transfusion history. These data also highlight the importance of monitoring for thrombotic events and major adverse events in patients with PNH. Additionally, data from the largest cohort of pediatric patients with PNH underscore that younger patients can also have a significant disease burden, including thrombotic events."

Mustafa Yenerel, M.D., Ph.D., of Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Hematology, Istanbul, Turkey, presented an analysis of disease progression in untreated patients with PNH during periods with and without hemolysis. In this analysis, 1,012 untreated patients were included in the cohort with no reported hemolysis, while 1,565 untreated patients were in the cohort with reported hemolysis. Symptoms of PNH, including abdominal pain, dyspnea, dysphagia, and erectile dysfunction, were more frequently reported among patients with hemolysis than those without ($p < 0.05$). There was a risk of thrombotic events (TEs) and major adverse vascular events (MAVEs) in both cohorts, however the annual rate of TEs, MAVEs, and death was higher in patients with hemolysis than in patients without hemolysis ($p < 0.05$).¹

In a separate poster, Antonio Almeida, M.D., Ph.D., of Serviço de Hematologia, Instituto Português de Oncologia de Lisboa, Francisco Gentil, Lisbon, Portugal, presented an analysis of the clinical benefits of Soliris in patients with and without a history of transfusion with a focus on patients with high disease activity (HDA) as defined by elevated hemolysis ($\text{LDH} \geq 1.5 \times \text{ULN}$) and the presence of related clinical symptom(s), such as fatigue, hemoglobinuria, abdominal pain, shortness of breath, anemia, MAVEs (including thrombosis), dysphagia or erectile dysfunction. The analysis included non-transfused untreated patients ($n=144$), non-transfused patients who were treated with Soliris ($n=45$), and patients who were treated with Soliris and had received ≥ 1 red blood cell transfusion in the six months prior to initiation of Soliris treatment ($n=105$). Researchers reported that patients treated with Soliris had statistically significant and clinically meaningful reductions in lactate dehydrogenase (LDH) and improvement in fatigue, regardless of transfusion history, and in patients with HDA. Non-transfused and transfused treated patients had mean absolute change in LDH of -1318.8 U/L and -1722.2 U/L , respectively, compared with -39.4 U/L in non-

transfused untreated patients ($p < 0.001$). These results are consistent with the established efficacy profile of Soliris in patients with a prior history of transfusion.²

In a third poster presentation, Álvaro Urbano-Ispuza, M.D., Ph.D., of the Hospital Clinic, University of Barcelona, Institute of Research Josep Carreras, Barcelona, Spain, reported outcomes from an analysis of disease characteristics at enrollment in the registry for pediatric patients with PNH ($n=99$) compared with those of adult patients ($n=2,268$). The registry represents the largest available pediatric cohort of PNH patients, and researchers concluded that this analysis demonstrates an important disease burden for this understudied population.³

Data from a Long-Term Follow-Up Study of Soliris in Patients with aHUS

Larry A. Greenbaum, M.D., Ph.D., of Emory University School of Medicine and Children's Healthcare of Atlanta, presented results from an ongoing, long-term follow-up study evaluating the rate and severity of TMA events during treatment with Soliris and following discontinuation of Soliris treatment in patients with aHUS. The study included 87 patients who had been treated with Soliris in any of five previous clinical studies. Seventy-six patients had on-treatment periods (median 26.1 months) and 39 patients had off-treatment periods (median 20.1 months) during this observational trial. Inclusive of time in the parent studies, patients had a median of 45.9 months of exposure to Soliris.

For the primary endpoint, researchers reported that the TMA event rate was 63 percent lower during periods of Soliris treatment compared to periods of treatment discontinuation. Additionally, the rate of TMA events during periods of on-label dosing of Soliris was 74 percent lower than during periods of treatment discontinuation and was also 57 percent lower compared with periods when patients were on treatment but receiving non-labeled dosing. Moreover, off-treatment periods were more frequently associated with serious adverse events and hospitalizations related to TMA events compared with on-treatment periods.⁴

There were no unexpected Soliris safety signals reported during the observational study period, and serious targeted adverse event rates were similar between on-treatment and off-treatment periods. One adult patient from parent study C10-004 died during the observational study due to intensive care complications and multi-organ failure determined to be caused by coexisting disease and unrelated to Soliris. Two patients from parent study C09-001 reported meningococcal infections during the observational study; both were determined to be probably related to Soliris. Both patients recovered and no changes to Soliris dosing were made.

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.⁵ Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger.⁶ 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.⁷ 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.⁵ PNH has been identified more commonly among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndromes (MDS).^{8,9,10} In patients with thrombosis of unknown origin, PNH may be an underlying cause.⁵

About the International PNH Registry

The International PNH Registry is a prospective, observational, non-interventional study of patients with a diagnosis of PNH or with a detected PNH clone, irrespective of disease severity or treatment status. The Registry is sponsored by Alexion and is overseen by an executive committee of international PNH experts. The goals of the Registry are to compile data on the progression of PNH, to assess the safety and effectiveness of PNH treatment options, and to optimize clinical decision-making through enhanced understanding of PNH and its treatments. The Registry initially began in 2004 as a natural history study and was updated in 2008 to include patients treated with Soliris. To date, more than 4,000 patients have been enrolled in the International PNH Registry.

About aHUS

aHUS is a chronic, ultra-rare, and life-threatening disease in which a life-long and permanent genetic deficiency in one or more complement regulatory genes causes chronic uncontrolled complement activation, resulting in complement-mediated thrombotic microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body.^{11,12} 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.^{11,13} Seventy-nine percent of all patients with aHUS die, require kidney dialysis or have permanent kidney damage within three years after diagnosis despite plasma exchange or plasma infusion (PE/PI).¹⁴ Moreover, 33 to 40 percent of patients die or progress to end-stage renal disease with the first clinical manifestation of aHUS despite PE/PI.^{14,15} The majority of patients with aHUS who receive a kidney transplant commonly experience subsequent systemic TMA, resulting in a 90 percent transplant failure rate in these aHUS patients.¹⁶

aHUS affects both children and adults. 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 to 50 percent of patients with a confirmed clinical diagnosis of aHUS.¹⁴

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.

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, and 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 global biopharmaceutical company focused on developing and delivering life-transforming therapies for patients with devastating and rare disorders. Alexion developed and commercializes Soliris® (eculizumab), 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. As the global leader in complement inhibition, Alexion is strengthening and broadening its portfolio of complement inhibitors, including evaluating potential indications for eculizumab in additional severe and ultra-rare disorders. Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, Strensiq™ (asfotase alfa) to treat patients with hypophosphatasia (HPP) and Kanuma™ (sebelipase alfa) to treat patients with lysosomal acid lipase deficiency (LAD). In addition, 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.

Forward-Looking Statements

This news release contains forward-looking statements, including statements related to potential medical benefits of Soliris® (eculizumab) in atypical hemolytic uremic syndrome (aHUS) and paroxysmal nocturnal hemoglobinuria (PNH). Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ from those expected, including for example, risks and uncertainties of drug development, 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, 2015 and Alexion's other filings with the SEC. 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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