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Alexion Initiates Simultaneous Registration Trials of ALXN1210 for Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) and Atypical Hemolytic Uremic Syndrome (aHUS)

-- Multinational Trials to Evaluate ALXN1210 Administered Every Eight Weeks in Patients with PNH and aHUS; Enrollment to Begin in Q4 -

-- ALXN1210 Subcutaneous Clinical Program Commenced with Dosing Underway in Healthy Volunteers in Phase I Study --

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced the initiation of two Phase 3 trials of ALXN1210, a highly innovative, longer-acting anti-C5 antibody that inhibits terminal complement. The first trial is a Phase 3 open-label, multinational, active-controlled study of ALXN1210 compared to eculizumab (Soliris[®]) in complement inhibitor treatment-naïve patients with paroxysmal nocturnal hemoglobinuria (PNH). Alexion has also accelerated the initiation of a registration trial of ALXN1210 in patients with atypical hemolytic uremic syndrome (aHUS). This second trial is a Phase 3, open-label, single arm, multinational trial to evaluate the safety and efficacy of ALXN1210 in complement inhibitor treatment-naïve adolescent and adult patients with aHUS. Both studies will evaluate ALXN1210 administered intravenously every eight weeks. Alexion expects to begin enrolling patients into these trials later this year, and plans to initiate a Phase 3 trial of ALXN1210 in pediatric patients with aHUS in 2017.

Alexion has also commenced dosing of a new formulation of ALXN1210 administered subcutaneously in healthy volunteers in a Phase I study.

PNH is a debilitating, ultra-rare and life-threatening blood disorder characterized by complement-mediated hemolysis (destruction of red blood cells).¹ aHUS is a genetic, chronic, ultra-rare disease associated with vital organ failure and premature death.^{2,3,4} Both PNH and aHUS are caused by chronic uncontrolled complement activation.

"With more than 20 years of expertise in the discovery and development of complement inhibitors, our ongoing commitment is to bring even higher levels of innovation to patients with devastating ultra-rare diseases," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "We are very pleased with our agreement with global regulators to progress ALXN1210 into Phase 3 studies in patients with PNH and aHUS and are now working with investigators to enroll patients into the registration studies with urgency."

About the ALXN1210 PNH Study

The PNH trial is a Phase 3, randomized, open-label, active-controlled, multicenter 26-week study to evaluate the safety and efficacy of ALXN1210 compared to eculizumab in complement inhibitor treatment-naïve patients with PNH. The co-primary endpoints are the normalization of lactate dehydrogenase (LDH) levels and the percentage of patients who achieve transfusion avoidance (TA). Secondary endpoints include percentage change from baseline in LDH levels, change from baseline in quality of life as assessed by the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue, and percentage of patients with stabilized hemoglobin. The study is designed to evaluate the non-inferiority of ALXN1210 compared to eculizumab.

Patients in the ALXN1210 arm will receive a single loading dose of ALXN1210, followed by regular maintenance dosing every 8 weeks based on 3 weight cohorts. Patients in the eculizumab arm will receive 4 weekly induction doses, followed by regular maintenance dosing every 2 weeks. The multinational study will enroll approximately 214 adults (≥ 18 years of age) with a diagnosis of PNH who have never been treated with a complement inhibitor.

About the ALXN1210 aHUS Study

The aHUS trial is a Phase 3, open-label, single arm, multicenter 26-week study to evaluate the safety and efficacy of ALXN1210 in complement inhibitor treatment-naïve adolescent and adult patients with aHUS. The primary endpoint is complete thrombotic microangiopathy (TMA) response at 26 weeks. Secondary endpoints include dialysis requirement status, complete TMA response over time, observed value and change from baseline in estimated glomerular filtration rate, and change from baseline in chronic kidney disease stage, all evaluated at 26 weeks; time to complete TMA response; and

additional efficacy measures. Patients will receive a single loading dose of ALXN1210, followed by regular maintenance dosing every 8 weeks based on 3 weight cohorts.

The multinational study will enroll approximately 55 adolescent (12 to < 18 years of age) and adult (\geq 18 years of age) patients with aHUS who have never been treated with a complement inhibitor.

About Paroxysmal Nocturnal Hemoglobinuria (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.¹ Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger.⁵ 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.⁶ In the period of time before Soliris[®] (eculizumab) 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.⁷ 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.¹¹

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.^{2,3} 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.^{2,4} Prior to the availability of Soliris, seventy-nine percent of all patients with aHUS died, required kidney dialysis or had permanent kidney damage within three years after diagnosis despite plasma exchange or plasma infusion (PE/PI).¹² Moreover, 33 to 40 percent of patients died or progressed to end-stage renal disease with the first clinical manifestation of aHUS despite PE/PI.^{12,13} Prior to the availability of Soliris, the majority of patients with aHUS who received a kidney transplant commonly experienced subsequent systemic TMA, resulting in a 90 percent transplant failure rate in these TMA patients.¹⁴

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 30-50 percent of patients with a confirmed diagnosis of aHUS.^{12,14,15}

About ALXN1210

ALXN1210 is a highly innovative, longer-acting anti-C5 antibody discovered and developed by Alexion that inhibits terminal complement. In early studies, ALXN1210 demonstrated rapid, complete, and sustained reduction of free C5 activity.¹⁶ Alexion has completed enrollment in two ongoing clinical studies of ALXN1210 in patients with PNH—a Phase 1/2 dose-escalating study and an open-label, multi-dose Phase 2 study that is also evaluating longer dosing intervals beyond 8 weeks.

ALXN1210 is currently in Phase 3 trials in patients with PNH and aHUS. In addition, Alexion is conducting a Phase 1 study to evaluate a new formulation of ALXN1210 administered subcutaneously in healthy volunteers.

In June 2016, the European Commission granted Orphan Drug Designation (ODD) to ALXN1210 for the treatment of patients with PNH.

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 is the global leader in complement inhibition and has developed and commercialized 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 Statement

This press release contains forward-looking statements, including statements related to Alexion's development plans for ALXN1210, the medical benefits of ALXN1210 for the treatment of PNH and aHUS, medical and commercial potential of ALXN1210, and plans for regulatory filings for ALXN1210. 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 current results of commercialization are not predictive of future rates of adoption of Soliris in PNH, aHUS or other diseases, the possibility that clinical trials of our product candidates could be delayed or that additional research and testing is required by regulatory agencies, including for ALXN1210, 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, the risk that anticipated regulatory filings are delayed, including for ALXN1210, the risk that estimates regarding the number of patients with PNH, aHUS, HPP and LAL-D 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.

References

1. Socié G, Mary JY, de Gramont A, et al. Paroxysmal nocturnal haemoglobinuria: long-term follow-up and prognostic factors. *Lancet*. 1996; 348:573-577.
2. Benz K, Amann K. Thrombotic microangiopathy: new insights. *Curr Opin Nephrol Hypertens*. 2010;19(3):242-7.
3. Ariceta G, Besbas N, Johnson S, et al. Guideline for the investigation and initial therapy of diarrhea-negative hemolytic uremic syndrome. *Pediatr Nephrol*. 2009;24:687-96.
4. Tsai HM. The molecular biology of thrombotic microangiopathy. *Kidney Int*. 2006;70(1):16-23.
5. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. *Blood*. 2005;106(12):3699-3709.
6. Dacie JV, Lewis SM. Paroxysmal nocturnal haemoglobinuria: clinical manifestations, haematology, and nature of the disease. *Ser Haemat*. 1972;5:3-23.
7. Hillmen P, Lewis SM, Bessler M, Luzzatto L, Dacie JV. Natural history of paroxysmal nocturnal hemoglobinuria. *N Engl J Med*. 1995;333(19):1253-1258.
8. Wang H, Chuhjo T, Yasue S, Omine M, Naka S. Clinical Significance of a minor population of paroxysmal nocturnal hemoglobinuria-type cells in bone marrow failure syndrome. *Blood*. 2002;100(12):3897-3902.
9. Iwanga M, Furukawa K, Amenomori T, et al. Paroxysmal nocturnal hemoglobinuria clones in patients with myelodysplastic syndromes. *Br J Haematol*. 1998;102(2):465-474.
10. Maciejewski JP, Rivera C, Kook H, Dunn D, Young NS. Relationship between bone marrow failure syndromes and the presence of glycosphosphatidyl inositol-anchored protein-deficient clones. *Br J Haematol*. 2001;115:1015-1022.
11. Hill A, Kelly RJ, Hillmen P. Thrombosis in paroxysmal nocturnal hemoglobinuria. *Blood*. 2013;121:4985-4996.
12. Noris M, Caprioli J, Bresin E, et al. Relative Role of genetic complement abnormalities in sporadic and familial aHUS and their impact on clinical phenotype. *Clin J Am Soc Nephrol*. 2010;5:1844-59.
13. 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.
14. Bresin E, et al. Combined Complement Gene Mutations in Atypical Hemolytic Uremic Syndrome Influence Clinical Phenotype. *J Am Soc Nephrol*. 2013;24: 475-486.
15. Fremeaux-Bacchi, et al. Genetics and Outcome of Atypical Hemolytic Uremic Syndrome: A Nationwide French Series Comparing Children and Adults. *Clin J Am Soc Nephrol*. 2013 Apr 5; 8(4): 554-562.
16. Sahelijo L, Mujeebuddin A, Mitchell D, et al. First in human single-ascending dose study: safety, biomarker, pharmacokinetics and exposure-response relationships of ALXN1210, a humanized monoclonal antibody to C5, with marked half-life extension and potential for significantly longer dosing intervals. *Blood*. 2015;126 (23):4777.

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