



December 4, 2016

New Data from ALXN1210 Dose-Escalation Study Presented at ASH Show Rapid and Sustained Reductions in LDH in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)

Recruitment Under Way in Multinational Phase 3 Trials of ALXN1210 Administered Every Eight Weeks in Patients with PNH and Atypical Hemolytic Uremic Syndrome (aHUS)

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq:ALXN) announced today that new data from an ongoing Phase 1/2 dose-escalation study of ALXN1210 in patients with paroxysmal nocturnal hemoglobinuria (PNH) showed rapid and sustained reductions in lactate dehydrogenase (LDH), a direct marker of hemolysis (the destruction of red blood cells), in patients treated with once-monthly dosing. In the interim analysis of 13 patients, reductions in LDH were observed at the first evaluable time point (week 1) and were sustained over the study analysis period of up to 24 weeks. Patients also had improvements in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score from baseline, with patients in the higher-dose cohort achieving a two-fold greater improvement compared with the lower-dose cohort.¹ These findings were presented in a poster session at the 58th American Society of Hematology (ASH) annual meeting in San Diego.

ALXN1210 is a highly innovative longer-acting anti-C5 antibody currently in Phase 3 trials in patients with PNH and atypical hemolytic uremic syndrome (aHUS). PNH is a debilitating, ultra-rare blood disorder characterized by complement-mediated hemolysis.² In patients with PNH, the combination of LDH ≥ 1.5 times the upper limit of normal with any one of the following clinical symptoms—abdominal pain, chest pain, dyspnea, hemoglobinuria, or fatigue—is associated with an increased risk of thromboembolism, the leading cause of death in PNH.³ aHUS is a genetic, chronic, ultra-rare complement-mediated disease associated with vital organ failure and premature death.^{4,5,6}

"As the global leader in complement biology, Alexion is committed to achieving the highest levels of innovation to address the needs of patients suffering from severe, ultra-rare complement-mediated disorders like PNH," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "Results from the Phase 1/2 study of ALXN1210 presented at ASH continue to support earlier findings that this highly innovative molecule has the potential to offer rapid, complete, and sustained complement inhibition for patients suffering from the devastating effects of PNH. We are now focused on enrolling patients with PNH and aHUS in our Phase 3 registration programs to evaluate ALXN1210 administered every eight weeks."

Immediate, Complete, and Sustained Inhibition of C5 with ALXN1210 Reduces Complement-Mediated Hemolysis in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH): Interim Analysis of a Dose-Escalation Study¹

In a poster session, researchers presented interim results from the Phase 1/2, open-label, 24-week dose-escalating study of ALXN1210 in patients with PNH. Initial findings from the study were previously reported at the 21st Congress of the European Hematology Association (EHA) in June 2016, demonstrating that ALXN1210 achieved rapid and sustained LDH reductions.⁷ The current analysis evaluated two cohorts of complement inhibitor-naïve patients with PNH (ages 18 and older; n=13) who had mean LDH levels ≥ 3 times the upper limit of normal. Patients in Cohort 1 (n=6) received either 400 mg or 600 mg induction doses of ALXN1210, followed by a 900 mg maintenance dose once-monthly for a median of 5.6 months. Patients in Cohort 2 (n=7) received 600 mg and 900 mg induction doses of ALXN1210, followed by an 1800 mg maintenance dose once-monthly for a median of 4.6 months.

All patients showed rapid reductions in mean LDH levels at Week 1 (the first evaluable time point), which were sustained over the study analysis period. As of the study analysis cutoff, treatment with ALXN1210 led to a mean reduction in LDH levels of 86 percent in Cohort 1 (baseline to Week 24) and 85 percent in Cohort 2 (baseline to Week 20). Four out of 6 patients in Cohort 1 (67 percent) and 4 out of 5 patients in Cohort 2 (80 percent) achieved LDH normalization, and 5 out of 6 patients in Cohort 1 (83 percent) and 5 out of 5 patients in Cohort 2 (100 percent) achieved mean LDH levels ≤ 1.5 times the upper limit of normal. Among five patients with one or more transfusions in the year prior to the study, one patient in Cohort 1 required a transfusion, while no patients in Cohort 2 required a transfusion with ALXN1210 treatment. In addition, mean levels of hemoglobin, another marker of intravascular hemolysis, were improved or stable in both cohorts.

Researchers also presented patient-reported changes in fatigue, as measured by the FACIT-Fatigue Scale. From baseline

to Week 24, mean FACIT-Fatigue score improved from 35.5 to 41.8 points (28.7 percent) for Cohort 1 and from 25.4 to 40.8 points (76.2 percent) for Cohort 2.

"In this interim analysis, ALXN1210 was associated with rapid and sustained reductions in LDH levels for up to six months in patients with PNH. Notably, patients in the higher-dose cohort had a 2-fold greater improvement in FACIT-Fatigue score, as well as no evidence of hemolysis or need for transfusion," said lead author Jong-Wook Lee, M.D., Ph.D., Professor, Division of Hematology, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea. "These findings are consistent with a better hemolytic response with the higher 1800 mg once-monthly dose and suggest that the 900 mg once-monthly dose may be inadequate in comparison with 1800 mg for complete suppression of complement-mediated hemolysis."

No serious adverse events or study withdrawals were observed in either patient cohort. The most common treatment-related adverse event was headache, which occurred in four of 13 patients (30.8 percent) and resolved during ongoing treatment with ALXN1210.

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 levels.⁸ 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 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.² Approximately 10 percent of all patients first develop symptoms at 21 years of age or younger.⁹ 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.¹⁰ In the period of time before treatment was available, it had been estimated that approximately one-third of patients with PNH did not survive more than 5 years from the time of diagnosis.¹¹ PNH has been identified more commonly among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndromes (MDS).¹²⁻¹⁴ In patients with thrombosis of unknown origin, PNH may be an underlying cause.¹⁵

About Atypical Hemolytic Uremic Syndrome (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.^{4,5} 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.^{4,6} 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).¹⁶ Moreover, 33-40 percent of patients die or progress to end-stage renal disease with the first clinical manifestation of aHUS despite PE/PI.^{17,18} 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 TMA patients.¹⁷

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 40-50 percent of patients with a confirmed diagnosis of aHUS.^{16,17,19}

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 Statements

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 materially 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, risks relating to the internal investigation being conducted by the Audit and Finance Committee, 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.

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