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Results of Phase 1b/2 Dose Regimen Optimization Studies for ALXN1210 in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Presented at American Society of Hematology (ASH) Meeting

-- Data Demonstrate Rapid and Sustained Reduction of Plasma Lactate Dehydrogenase (LDH) --

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) announced today the presentation of comprehensive dose-ranging data from two Phase 1b/2 studies of ALXN1210, the Company's investigational long-acting C5 complement inhibitor, in patients with paroxysmal nocturnal hemoglobinuria (PNH), a chronic, progressive, debilitating and potentially life-threatening ultra-rare blood disorder characterized by complement-mediated hemolysis.[1,2] Treatment with ALXN1210 for up to eight months resulted in rapid and sustained reduction of plasma lactate dehydrogenase (LDH) levels, a direct marker of hemolysis, with reductions in mean LDH levels from Baseline (BL) ranging from 73% to 88%. ALXN1210 was generally well tolerated with a safety profile that is consistent with that seen historically in patients with complement inhibition.[3] The data were presented at the 59th American Society of Hematology (ASH) Annual Meeting & Exposition in Atlanta. All patients from the Phase 1b study and from Cohorts 1, 2, and 3 of the Phase 2 study have been successfully transitioned to the Phase 3 dosing regimen, after which plasma LDH levels have remained suppressed.

"It is encouraging to see rapid and sustained reduction in plasma LDH levels in these dose optimization studies," said Alexander Röth, M.D. from the Department of Hematology, West German Cancer Center, University Hospital Essen, Essen, Germany and an investigator in the Phase 1b/2 studies. "These comprehensive results provide robust preliminary evidence for the efficacy and safety of ALXN1210 as a future treatment for patients with PNH."

"The strength of these data and exposure-response analyses, along with the totality of data for ALXN1210 and discussions with global regulators, allowed us to determine an eight-week, weight-based dosing regimen that targets complete C5 inhibition and rapid and sustained suppression of LDH," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "We have completed enrollment in our two multinational Phase 3 PNH studies, with nearly 450 patients enrolled, and expect data from these studies in the second quarter of 2018."

Optimization of Dose Regimen for ALXN1210, a Novel Complement C5 Inhibitor, in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH): Results of Two Phase 1b/2 Studies[3]

The researchers presented results from two open-label Phase 1b/2 studies designed to provide dose ranging data to optimize the dosing regimen for the Phase 3 development of ALXN1210 as a treatment for patients with PNH based on exposure-response assessments. The studies included a total of 39 adult patients with PNH (Study 103, n=13; Study 201, n=26) who were naïve to complement inhibition. The primary efficacy endpoint was the change from BL in mean plasma LDH levels to day 169 in Study 103 and day 253 in Study 201. The secondary efficacy endpoints were changes from BL in free hemoglobin, haptoglobin, and reticulocytes. Post hoc efficacy analyses evaluated the proportion of patients achieving LDH levels within the normal range and the incidence of breakthrough hemolysis (days 29-253). LDH BL was defined as the average of values at screening, prior to the first ALXN1210 infusion. For other parameters, BL was defined as the most recent value prior to the first infusion. Study 103 evaluated two escalating intravenous (IV) dosing regimens of ALXN1210, and Study 201 evaluated four IV regimens with different doses and intervals. The results demonstrated exposure-response relationships, and further substantiate and extend previously presented results.[4,5,6,7]

	Study 201				Study 103	
LDH at Protocol-Specified Endpoint[a]	Cohort 1 1000 mg q4w n=6	Cohort 2 1600 mg q6w n=6	Cohort 3 2400 mg q8w n=7	Cohort 4 5400 mg q12w n=7	Cohort 1 900 mg q4w n=6	Cohort 2 1800 mg q4w n=7
% LDH reduction from BL, mean (SD)[b]	72.9 (12.1)	77.8 (6.5)	85.0 (4.4)	87.6 (6.9)	86.0 (3.2)	84.7 (3.8)
LDH levels, U/L, mean (SD)	230.0 (44.0)	266.0 (54.3)	306.1 (130.7)	276.4 (196.9)	232.0 (82.3)	227.9 (50.6)
LDH normalization (D29-D253)[c]						
LDH normalized, n/N (%)	5/6 (83)	3/6 (50)	4/7 (57)	5/7 (71)	4/6 (67)	6/7 (86)

LDH > 1.5 x ULN, n/N (%)	4/6 (67)	3/6 (50)	2/7 (29)	3/7(43)	2/6 (33)	1/7 (14)
LDH > 2 x ULN, n/N (%)	2/6 (33)	1/6 (17)	2/7 (29)	1/7 (14)	1/6 (17)	0/7 (0)
Breakthrough hemolysis (D29-253)[d]						
Incidence of breakthrough hemolysis through day 253, n/N (%)	2/6 (33.3)	1/6 (16.7)	2/7 (28.6)	1/7 (14.3)	1/6 (16.7)	0/7 (0)

BL: baseline; SD: standard deviation; D: day; LDH: lactate dehydrogenase; ULN: upper limit of normal
q4w: every 4 weeks; q6w: every 6 weeks; q8w: every 8 weeks; q12w: every 12 weeks

[a] LDH parameters at protocol-specified endpoint: Study 103, day 169/24 weeks; Study 201, day 253/36 weeks.

[b] Primary efficacy endpoint.

[c] Patients meeting each parameter at least once after day 29 through day 253.

[d] Defined as at least 1 symptom or sign of intravascular hemolysis (fatigue, abdominal pain, shortness of breath [dyspnea], anemia [hemoglobin < 10 g/dL and hemoglobin < baseline hemoglobin], major adverse vascular event [including thrombosis], dysphagia, or erectile dysfunction) within ±7 days of an elevated LDH ≥2 x ULN after prior LDH reduction to < 1.5 x ULN on therapy.

The most frequent related treatment-emergent adverse event (TEAE) was headache. No patient stopped treatment or withdrew from the studies, and there were no deaths. Two patients in Study 201 experienced meningococcal infections but recovered completely and continued receiving ALXN1210. Meningococcal infections are a known risk with terminal complement inhibition, and specific risk-management plans have been in place for ten years for Soliris® (eculizumab) to minimize the risk for patients.

About Paroxysmal Nocturnal Hemoglobinuria (PNH)

Paroxysmal nocturnal hemoglobinuria (PNH) is a chronic, progressive, debilitating and potentially life-threatening ultra-rare blood disorder that can strike men and women of all races, backgrounds, and ages without warning, with an average age of onset in the early 30s.[1,2,8] PNH often goes unrecognized, with delays in diagnosis ranging from one to more than 10 years.[2] In patients with PNH, chronic, uncontrolled activation of the complement system, a component of the body's immune system, results in hemolysis (the destruction of red blood cells)[9], which in turn can result in progressive anemia, fatigue, dark urine and shortness of breath.[10,11,12] The most devastating consequence of chronic hemolysis is thrombosis (the formation of blood clots), which can damage vital organs and cause premature death.[13] Historically, it had been estimated that one in three patients with PNH did not survive more than five years from the time of diagnosis.[2] PNH is more common among patients with disorders of the bone marrow, including aplastic anemia (AA) and myelodysplastic syndromes (MDS).[14,15,16] In certain patients with thrombosis of unknown origin, PNH may be an underlying cause.[9]

About ALXN1210

ALXN1210 is an innovative, long-acting C5 inhibitor discovered and developed by Alexion that works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system that, when activated in an uncontrolled manner, plays a role in severe ultra-rare disorders like paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and anti-acetylcholine receptor (AchR) antibody-positive myasthenia gravis (MG). In early studies, ALXN1210 demonstrated rapid, complete, and sustained reduction of free C5 levels, as well as rapid and sustained reduction of plasma lactate dehydrogenase (LDH) levels, a direct marker of hemolysis (the destruction of red blood cells).[4,5,6,7] ALXN1210 is currently being evaluated in Phase 3 clinical studies as a potential treatment for patients PNH and aHUS, administered intravenously every eight weeks. In addition, Alexion plans to initiate a single, pharmacokinetics (PK)-based Phase 3 clinical study of ALXN1210 delivered subcutaneously once per week as a potential treatment for patients with PNH and aHUS.

ALXN1210 has received Orphan Drug Designation (ODD) for the intravenous treatment of patients with PNH in the U.S. and EU, and for the subcutaneous treatment of patients with aHUS in the U.S.

About Soliris® (eculizumab)

Soliris® is a first-in-class complement inhibitor that works by inhibiting the C5 protein in the terminal part of the complement cascade, a part of the immune system that, when activated in an uncontrolled manner, plays a role in severe rare and ultra-rare disorders like paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and anti-acetylcholine receptor (AchR) antibody-positive myasthenia gravis (MG). Soliris is approved in the U.S., EU, Japan, and other countries as the first and only treatment for patients with PNH and aHUS, in the EU as the first and only treatment of

refractory generalized MG (gMG) in adults who are anti-AchR antibody-positive, and in the U.S. for the treatment of adult patients with gMG who are anti-AchR antibody-positive. Alexion's new drug application in Japan for Soliris as a treatment for patients with anti-AchR antibody-positive refractory gMG has been accepted for review by the Japanese Ministry of Health, Labour, and Welfare (MHLW). Soliris is not indicated for the treatment of patients with Shiga-toxin E. coli-related hemolytic uremic syndrome (STEC-HUS).

Soliris has received Orphan Drug Designation (ODD) for the treatment of patients with PNH in the U.S., EU, Japan, and many other countries, for the treatment of patients with aHUS in the U.S., EU, and many other countries, for the treatment of patients with MG in the U.S. and EU, and for the treatment of patients with refractory gMG in Japan. Alexion and Soliris have received some of the pharmaceutical industry's highest honors for the medical innovation in complement inhibition: the Prix Galien USA (2008, Best Biotechnology Product) and France (2009, Rare Disease Treatment).

For more information on Soliris, please see full prescribing information for Soliris, including BOXED WARNING regarding risk of serious meningococcal infection, available at www.soliris.net

Important Soliris Safety Information

The U.S. prescribing information for Soliris includes the following warnings and precautions: 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 Centers for Disease Control (CDC)'s Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies. Immunize patients with meningococcal vaccines 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. 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. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-SOLIRIS (1-888-765-4747) or at www.solirisrems.com.

Patients may have increased susceptibility to infections, especially with encapsulated bacteria. Aspergillus infections have occurred in immunocompromised and neutropenic patients. Children treated with Soliris may be at increased risk of developing serious infections due to *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib). 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. Administration of Soliris may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions.

In patients with PNH, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, nasopharyngitis, back pain and nausea. 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. In patients with gMG who are anti-AchR antibody-positive, the most frequently reported adverse reaction observed with Soliris treatment in the placebo-controlled clinical study (≥10%) was musculoskeletal pain.

About Alexion

Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases through the innovation, development, and commercialization of life-changing therapies. Alexion is the global leader in complement inhibition and has developed and commercializes the first and only approved complement inhibitor to treat patients with paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and anti-acetylcholine receptor (AchR) antibody-positive generalized myasthenia gravis (gMG). In addition, Alexion has two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare metabolic disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). As the leader in complement biology for over 20 years, Alexion focuses its research efforts on novel molecules and targets in the complement cascade, and its development efforts on the core therapeutic areas of hematology, nephrology, neurology, and metabolic disorders. 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 the potential medical benefits of ALXN1210 for the treatment of PNH. Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ from those expected, including for example, the risks and uncertainties of drug development, decisions of regulatory authorities regarding the adequacy of our research, 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, failure to satisfactorily address matters raised by the FDA and other regulatory agencies, the possibility that the current rates of adoption of Soliris in paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), or other diseases are not sustained, the possibility that results of clinical trials are not predictive of safety and efficacy results of our products in broader patient populations, the possibility that clinical trials of our product candidates could be delayed, the adequacy of our pharmacovigilance and drug safety reporting processes, the risk that third party payers (including governmental agencies) will not reimburse or continue to reimburse for the use of our products at acceptable rates or at all, the outcome of challenges and opposition proceedings to our intellectual property, assertion or potential assertion by third parties that the manufacture, use or sale of our products infringes their intellectual property, uncertainties surrounding legal proceedings, company investigations and government investigations, including investigations of Alexion by the U.S. Securities and Exchange Commission (SEC) and U.S. Department of Justice (DOJ), the risk that anticipated regulatory filings are delayed, the risk that estimates regarding the number of patients with PNH, aHUS, gMG, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D) are inaccurate, the risks of changing foreign exchange rates, risks relating to the potential effects of the Company's restructuring and relocation of its corporate headquarters, and a variety of other risks set forth from time to time in Alexion's filings with the SEC, including but not limited to the risks discussed in Alexion's Quarterly Report on Form 10-Q for the period ended September 30, 2017 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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