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Alexion Announces Positive Top-Line Results Showing Successful Phase 3 Clinical Study of ALXN1210 in Complement Inhibitor Treatment-Naïve Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)

-- ALXN1210 Achieved Non-Inferiority to Soliris[®] (Eculizumab) on Co-Primary Endpoints of Transfusion Avoidance and Lactate Dehydrogenase Normalization, and All Four Key Secondary Endpoints --

-- Safety Profile of ALXN1210 Consistent with That Seen for Soliris[®] --

-- Regulatory Submissions Planned in the United States, European Union, and Japan in the Second Half of 2018 --

-- Conference Call/Webcast Scheduled for Today, Thursday, March 15, 2018 at 8:30 a.m. EDT --

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ: ALXN) announced today that the pivotal Phase 3 study of ALXN1210, the Company's investigational long-acting C5 complement inhibitor, demonstrated non-inferiority to Soliris[®] (eculizumab) in complement inhibitor treatment-naïve patients with paroxysmal nocturnal hemoglobinuria (PNH) based on the co-primary endpoints of transfusion avoidance and normalization of lactate dehydrogenase (LDH) levels, a direct marker of complement-mediated hemolysis in PNH. The study also demonstrated non-inferiority on all four key secondary endpoints: 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 scale, proportion of patients with breakthrough hemolysis, and proportion of patients with stabilized hemoglobin levels. In addition, numeric results for all six endpoints favored ALXN1210. There were no notable differences in the safety profiles for ALXN1210 and Soliris[®].

Endpoint	Treatment effect [95% CI: LB,UB]		Treatment difference ALXN1210 vs. Soliris [®] [95% CI: LB,UB]	Non-inferiority	
	ALXN1210 n=125	Soliris [®] n=121		Requirement	Achieved*
<i>Primary</i>					
Transfusion avoidance	73.6% [65.9%,81.3%]	66.1% [57.7%,74.6%]	6.8% [-4.7%,18.1%] ^a	LB > -20%	Yes
LDH normalization	53.6% [45.9%,61.2%]	49.4% [41.7%,57.0%]	1.19 [0.80,1.77] ^b	LB > 0.39	Yes
<i>Secondary</i>					
Change in LDH levels	-76.8% [-80.0%,- 73.7%]	-76.0% [-79.2%,- 72.8%]	-0.83% [-5.2%,3.6%] c,†	UB < 20%	Yes
Improvement in FACIT scale	7.1 [5.6,8.6]	6.4 [4.9,8.0]	0.67 [-1.2,2.6] ^c	LB > -5.0	Yes
Breakthrough hemolysis	4.0% [0.6%,7.4%]	10.7% [5.2%,16.3%]	-6.7% [- 14.2%,0.18%] ^{a,†}	UB < 20%	Yes
Stabilization of Hb levels	68.0% [59.8%,76.2%]	64.5% [55.9%,73.0%]	2.9% [-8.8%,14.6%] ^a	LB > -20%	Yes

LDH: lactate dehydrogenase; FACIT: Functional Assessment of Chronic Illness Therapy; Hb: hemoglobin; CI: confidence interval; LB: lower bound; UB: upper bound

* Non-inferiority is achieved if the LB or UB of the 95% CI of the treatment difference meets the pre-defined requirement. Since non-inferiority

was achieved across both co-primary and all four key secondary endpoints, the protocol allowed for superiority testing. Testing for superiority followed a closed-testing procedure, using a 2-sided 0.05 test for each parameter, and followed the pre-specified order per protocol: breakthrough hemolysis, change in LDH levels vs. Baseline, LDH normalization, improvement in FACIT scale, stabilization of Hb levels, transfusion avoidance. As breakthrough hemolysis did not achieve statistical significance (p-value = 0.074), no other endpoints were tested.

a) Difference in proportion of patients; b) Odds ratio; c) Difference in change vs. Baseline

† Negative value meaning a difference in favor of ALXN1210

Since non-inferiority was achieved across both co-primary and all four key secondary endpoints, the protocol allowed for superiority testing. The hierarchical testing order pre-specified breakthrough hemolysis as the first endpoint tested for superiority. Although ALXN1210 did not achieve superiority, a numeric trend in favor of ALXN1210 was observed for breakthrough hemolysis (4.0% [0.6%,7.4%] vs. 10.7% [5.2%,16.3%] for Soliris[®]) with a p-value of 0.074. The study also confirmed that ALXN1210 provides immediate and complete (> 99%) inhibition of the complement C5 protein that is sustained over the entire 8 week dosing interval. Additionally, treatment with ALXN1210 reduced mean LDH levels to approximately the upper limit of normal (1.0-1.1 times ULN) between months one and six.

"We are very pleased with these positive data for ALXN1210 in the first and only head-to-head study versus Soliris, and the results reinforce our ambition to establish ALXN1210 as the new standard of care for patients with PNH. The data are also consistent with our hypothesis that immediate, complete, and sustained C5 inhibition is critical for patients with this potentially life-threatening disease," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "Soliris has established a high bar for efficacy. Achieving non-inferiority on both co-primary and all key secondary endpoints, as well as seeing numeric results in favor of ALXN1210, in such a rigorous study met a very high hurdle. We look forward to regulatory submissions of ALXN1210 in PNH in the U.S., EU, and Japan in the second half of 2018."

"Having a new treatment option that achieves transfusion avoidance, and provides rapid and sustained normalization of LDH levels when administered 6 times a year could be a meaningful improvement for patients with PNH who currently need 26 infusions per year," said Jong Wook Lee, M.D., Professor of Internal Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea, and an investigator in the ALXN1210 study.

ALXN1210 was generally well tolerated with a safety profile that is consistent with that seen for Soliris[®]. The most frequently observed adverse event was headache. The most frequently observed serious adverse event was pyrexia. One patient in the Soliris[®] arm died from lung cancer (unrelated to Soliris[®] treatment) during the extension phase of the study. Two patients withdrew from the Soliris[®] arm for reasons unrelated to treatment. One anti-drug antibody was observed for ALXN1210 and one for Soliris[®]. No neutralizing antibodies and no apparent effects on efficacy, safety, pharmacokinetics, or pharmacodynamics were detected. There were no cases of meningococcal infection observed in either the ALXN1210 or Soliris[®] arms. Meningococcal infections are a known risk with terminal complement inhibition, and specific risk-mitigation plans have been in place for ten years for Soliris[®] to minimize the risk for patients.

Detailed results from this Phase 3 study will be presented at a future medical congress.

About the ALXN1210-PNH-301 Study

This Phase 3, randomized, open-label, active-controlled, multinational, and multicenter study evaluated the efficacy and safety of ALXN1210 compared to Soliris[®] administered by intravenous (IV) infusion to adult patients (≥ 18 years of age) with PNH who are naïve to complement inhibitor treatment. The study enrolled 246 adult patients with a confirmed diagnosis of PNH who had never been treated with a complement inhibitor and presented with LDH levels ≥ 1.5 times the upper limit of normal (ULN) at the time of screening, as well as with one or more of the following PNH-related signs or symptoms within 3 months of screening: fatigue, hemoglobinuria, abdominal pain, shortness of breath (dyspnea), anemia (hemoglobin < 10 g/dL), history of a major adverse vascular event (MAVE, including thrombosis), dysphagia, or erectile dysfunction; or history of packed red blood cell (pRBC) transfusion due to PNH. Patients in the ALXN1210 arm received a single loading dose of ALXN1210, followed by regular maintenance weight-based dosing every 8 weeks. Patients in the Soliris[®] arm received 4 weekly induction doses, followed by regular maintenance dosing every 2 weeks. Both arms were treated for 26 weeks. The study was designed to evaluate the non-inferiority of ALXN1210 compared to Soliris[®].

The co-primary endpoints were the proportion of patients who remain transfusion-free and do not require a transfusion per

protocol-specified guidelines through day 183 and the normalization of LDH levels as directly measured every two weeks by LDH levels ≤ 1 times ULN from day 29 through day 183. Key secondary endpoints included the percentage change from baseline in LDH levels to day 183, change from baseline in quality of life as assessed by the FACIT-Fatigue scale to day 183, proportion of patients with breakthrough hemolysis, and proportion of patients with stabilized hemoglobin levels (defined as avoidance of a ≥ 2 g/dL decrease in hemoglobin level from baseline in the absence of transfusion through day 183). Breakthrough hemolysis was defined as at least one new or worsening symptom or sign of intravascular hemolysis: fatigue, hemoglobinuria, abdominal pain, shortness of breath (dyspnea), anemia [hemoglobin < 10 g/dL], MAVE (including thrombosis), dysphagia, or erectile dysfunction in the presence of an elevated LDH level ≥ 2 times ULN, after prior LDH level reduction to < 1.5 times ULN on therapy. Blood samples for the determination of free and total complement C5 protein were collected before and after administration of study drug once a week during the first 4 weeks and every two weeks after that.

All patients enrolled in an extension study of up to 2 years, during which they will receive ALXN1210 every 8 weeks.

Conference Call

Alexion will host a conference call/webcast today, Thursday, March 15, 2018 at 8:30 a.m. EDT to discuss the study data. To participate in this call, dial (866) 762-3111 (USA) or +1 (210) 874-7712 (International), passcode 7686417, shortly before 8:30 a.m. EDT. A replay of the call will be available for a limited period of time following the call. The replay number is (855) 859-2056 (USA) or +1 (404) 537-3406 (International), passcode 7686417. The audio webcast can be accessed on the Investors page of Alexion's website at: <http://ir.alexion.com>.

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.^{1,2,3} 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)⁴, which in turn can result in progressive anemia, fatigue, dark urine, and shortness of breath.^{5,6,7} The most devastating consequence of chronic hemolysis is thrombosis (the formation of blood clots), which can damage vital organs and cause premature death.⁸ 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).^{9,10,11} In certain patients with thrombosis of unknown origin, PNH may be an underlying cause.⁴

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 a Phase 3 clinical study in complement inhibitor-naïve patients with PNH, intravenous treatment with ALXN1210 every 8 weeks demonstrated non-inferiority to treatment with Soliris[®] every 2 weeks. ALXN1210 is also currently being evaluated in a Phase 3 clinical study in patients with PNH who have been treated with Soliris[®] and in a Phase 3 clinical study in complement inhibitor-naïve patients with 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. Alexion also plans to initiate the development of ALXN1210 as a potential treatment for patients with generalized MG (gMG) and patients with immunoglobulin A nephropathy (IgAN).

ALXN1210 has received Orphan Drug Designation (ODD) for the 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, in the U.S. for the treatment of adult

patients with gMG who are anti-AchR antibody-positive, and in Japan for the treatment of patients with gMG who are AChR antibody-positive and whose symptoms are difficult to control with high-dose intravenous immunoglobulin (IVIg) therapy or plasmapheresis (PLEX). 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 influenzae* 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 commercialized 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.

[ALXN-G]

Forward-Looking Statement

This press release contains forward-looking statements, including statements related to Alexion's development plans for ALXN1210, the potential medical benefits of ALXN1210 for the treatment of PNH, and Alexion's future clinical, regulatory, and commercial plans 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 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 results of clinical trials are not predictive of safety and efficacy results of our products in broader patient populations, the possibility that current rates of adoption of our products are not sustained, 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 payors (including governmental agencies) will not reimburse or continue to reimburse for the use of our products at acceptable rates or at all, the possibility that expected tax benefits will not be realized, assessment of impact of recent accounting pronouncements, potential declines in sovereign credit ratings or sovereign defaults in countries where we sell our products, delay of collection or reduction in reimbursement due to adverse economic conditions or changes in government and private insurer regulations and approaches to reimbursement, 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, the risk that anticipated regulatory filings are delayed, the risk that estimates regarding the number of patients with the diseases that our products treat are inaccurate, the risks of changing foreign exchange rates, risks relating to the potential effects of Alexion'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 Annual Report on Form 10-K for the period ended December 31, 2017 and in our 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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