



Alexion Announces Successful Phase 3 PREVENT Study of Soliris® (Eculizumab) in Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD)

September 24, 2018

-- Soliris® Reduced the Risk of Adjudicated On-Trial Relapse by 94.2% Compared to Placebo ($p < 0.0001$) --

-- Safety Profile Consistent with that Seen in Previous Studies and Real-World Use --

-- Preparing for Regulatory Submissions in the US, European Union, and Japan --

-- Conference Call/Webcast Scheduled for Today, Monday, September 24, 2018 at 8:30 a.m. EDT --

BOSTON--(BUSINESS WIRE)--Sep. 24, 2018-- [Alexion Pharmaceuticals, Inc.](#) (NASDAQ: ALXN) today announced positive topline results from the Phase 3 PREVENT study of Soliris® (eculizumab) in patients with anti-aquaporin-4 (AQP4) auto antibody-positive neuromyelitis optica spectrum disorder (NMOSD). NMOSD is a rare, devastating, complement-mediated disorder of the central nervous system characterized by relapses. Each relapse results in stepwise accumulation of disability, including blindness and paralysis, and sometimes premature death.^{1,2,3} Patients who have anti-AQP4 auto-antibodies represent approximately three quarters of all patients with NMOSD.^{4,5,6,7} There are currently no approved therapies for this disease.

The study met its primary endpoint of time to first adjudicated on-trial relapse, demonstrating that treatment with Soliris® reduced the risk of NMOSD relapse by 94.2 percent compared to placebo ($p < 0.0001$). At 48 weeks, 97.9 percent of patients receiving Soliris® were free of relapse compared to 63.2 percent of patients receiving placebo. Soliris® was generally well tolerated with a safety profile consistent with that seen in previous clinical studies and real-world use in its three approved indications. No cases of meningococcal infection were observed.

"These results far exceeded our expectations. The remarkable reduction in relapse risk demonstrates the unique ability of Soliris® to inhibit complement, and suggests a promising new treatment for NMOSD," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "Given that patients currently have no approved therapies, we are moving quickly to discuss these results with regulators and file for approval in the U.S., EU, and Japan."

"The primary goal in treating NMOSD is relapse prevention as each relapse further increases disability, which makes this disease so devastating. For decades, we have been hoping for a therapy that can prevent relapse and subsequent accumulation of disability by addressing a critical underlying cause of the disease," said Michael Levy, M.D., Ph.D., Associate Professor at Johns Hopkins University, and Director of the Neuromyelitis Optica Clinic in Baltimore, MD. "The substantial effect of Soliris® seen in this groundbreaking randomized, controlled study in NMOSD could potentially become a turning point for patients and their families who live in constant fear of relapse."

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

About NMOSD

NMOSD is a rare, devastating, complement-mediated disorder of the central nervous system (CNS). Patients experience an unpredictable, relapsing, and deteriorating course of disease with each relapse adding to the disability, and potentially leading to premature death. Optic neuritis can cause eye pain and blindness. Transverse myelitis can cause severe weakness, impaired mobility, sensory and motor disability, loss of bowel and bladder function, paralysis, and respiratory failure.^{3,8,9} Significant proportions of patients sustain permanent severe disability, including blindness and paralysis, or die within six years (75 months) of disease onset. Specifically, one third (34 percent) of patients sustain permanent motor disability, almost one quarter (23 percent) become wheelchair-dependent, almost one fifth (18 percent) suffer from permanent visual disability, and almost one in 10 (9 percent) die.¹⁰

Patients with anti-aquaporin-4 (AQP4) auto-antibodies represent approximately three quarters of all patients with NMOSD.^{4,5,6,7} The disease primarily affects women.¹¹ There are currently no approved therapies for this disease.

In patients with NMOSD, the body's own immune system can turn on itself to produce auto-antibodies (immunoglobulin G [IgG]) against AQP4, a protein on certain cells in the brain and spinal cord that are critical for the survival of nerve cells. The binding of these anti-AQP4 auto-antibodies activates the complement cascade, another part of the immune system. Complement activation by anti-AQP4 auto-antibodies leads to destruction of vital cells in the CNS, leading to demyelination and to the death of neurons, predominantly in the spinal cord and optic nerve, which ultimately results in blindness, paralysis, and sometimes death.^{12,13,14,15,16}

About the PREVENT Study

The Prevention of Relapses and Evaluation of Eculizumab in NMOSD Treatment (PREVENT) study was a multinational, double-blind, parallel-group Phase 3 time-to-event study that assessed the efficacy and safety of Soliris® (eculizumab) compared to placebo for the treatment of patients with anti-aquaporin-4 (AQP4) auto antibody-positive neuromyelitis optica spectrum disorder (NMOSD). The study enrolled 143 adult patients who were randomized 2:1 to the Soliris® and placebo treatment arms. Patients needed to have a confirmed diagnosis of NMOSD, be seropositive for anti-AQP4 auto-antibodies (also called NMO-immunoglobulin G [IgG] antibodies), and have a history of at least two relapses in the last 12 months or three relapses in the last 24 months, with at least one relapse in the 12 months prior to screening. Patients were allowed to receive stable maintenance dose of protocol permitted supportive immune suppressive therapies for relapse prevention.

The primary endpoint was the time to first on-trial relapse as adjudicated by an independent committee comprised of three external experts in neurology/neuro-ophthalmology who were blinded to treatment. Adjudication decisions were based on objective and consistent clinical criteria described in a relapse adjudication charter. Secondary endpoints included adjudicated on-trial annualized relapse rate, and others assessing disability and quality of life, as well as safety and tolerability measures. Pre-specified sensitivity analyses include various types of statistical analyses of the time to relapse, and of secondary endpoints.

The study met its primary endpoint of time to first adjudicated on-trial relapse, demonstrating that treatment with Soliris[®] reduced the risk of NMOSD relapse by 94.2 percent compared to placebo ($p < 0.0001$). At 48 weeks, 97.9 percent of patients receiving Soliris[®] were free of relapse compared to 63.2 percent of patients receiving placebo. Treatment with Soliris[®] reduced the adjudicated on-trial annualized relapse rate compared to placebo, a key secondary endpoint, by 95.5 percent ($p < 0.0001$).

While results favored Soliris[®] on the other secondary endpoints, which included disability and quality of life measures, the observed differences were small. This was not unexpected since disease worsening in NMOSD is driven by damage incurred following relapse. Follow-up for assessment of long-term disability was limited by the trial design, which permitted patients to transition to the open-label study six weeks after the relapse, where all patients received Soliris[®]. Soliris[®] was generally well tolerated with a safety profile consistent with that seen in previous clinical studies and real-world use in its three approved indications. No cases of meningococcal infection were observed.

The treatment duration for an individual patient varied as this was a time-to-event study. Patients who completed the study either because of a relapse or because the study ended were provided with the opportunity to enter an extension study to receive open-label Soliris[®]. One hundred and nineteen patients entered the extension study.

Conference Call

Alexion will host a conference call/webcast today, Monday, September 24, 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 1296796, 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 audio webcast can be accessed on the Investors page of Alexion's website at: <http://ir.alexion.com>.

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, for the treatment of patients with refractory gMG in Japan, and for the treatment of patients with NMOSD in the U.S., EU, and 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 ($\geq 10\%$) was musculoskeletal pain.

About Alexion

Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases through the discovery, development, and commercialization of life-changing therapies. As the global leader in complement biology and inhibition for more than 20 years,

Alexion 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). Alexion also 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). In addition, the company is developing two late-stage therapies, a second complement inhibitor and a copper-binding agent for Wilson disease. 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. Alexion has been named to the *Forbes* list of the World's Most Innovative Companies seven years in a row and is headquartered in Boston, Massachusetts' Innovation District. The company also has offices around the globe and serves patients in more than 50 countries. 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" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements related to: the impact that the relapse reduction could have for patients with NMOSD using Soliris[®], complement inhibition can play a critical role in treating NMOSD, Soliris[®] may be a promising new treatment for NMOSD and a turning point in the treatment of this condition for patients and their families, the future planned submission of regulatory applications for review and approval by regulatory authorities in the U.S., the European Union and Japan for Soliris[®] as a treatment for NMOSD, future plans to present additional results and findings from Phase 3 of the PREVENT Study, and the potential medical benefits of Soliris[®] for the treatment of NMOSD and other diseases. Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ materially from those expected by these forward looking statements, including for example: the inability to submit regulatory applications for Soliris[®] as a treatment for NMOSD for review and approval by certain governmental authorities (or an unexpected delay in the timeframes for such submissions) due to increased expense, manufacturing delays or other reasons, the possibility that results of clinical trials are not predictive of safety and efficacy results of our products in broader patient populations (including Soliris[®] as a treatment for NMOSD), the inability to timely provide (or provide at all) the product safety and efficacy information required by regulatory authorities for Soliris[®] as a treatment for NMOSD, our products not gaining acceptance among patients (and providers or third party payers) for certain indications (due to cost or otherwise), the inability to develop future clinical study programs for certain product delivery mechanisms (or the failure of those programs to meet safety and efficacy goals), unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects, the inability to timely and cost-effectively develop programs for existing products for new indications (or the failure to obtain regulatory approval for use in such new indications), the introduction of competing drugs and product candidates for NMOSD, decisions of regulatory authorities regarding the adequacy of our research, marketing approval or material limitations on the marketing of our products (or the indications of such 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 current rates of adoption of our products are not sustained (or do not meet expected future rates), 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 (or proposed future products) at acceptable rates or at all, 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 other anticipated regulatory filings are delayed, the risk that estimates regarding the number of patients with the diseases that our products treat are inaccurate, 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 June 30, 2018 and in Alexion's other filings with the SEC. Alexion disclaims any obligation 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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