



New England Journal of Medicine Publishes Positive Phase 3 PREVENT Data for SOLIRIS® (eculizumab) in Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD)

May 3, 2019

- New data published in *NEJM* confirm sustained three-year treatment effect -

- Data will also be presented in Emerging Science session at American Academy of Neurology Annual Meeting -

- SOLIRIS for NMOSD currently under regulatory review in the U.S., European Union and Japan; U.S. FDA Priority Review action date of June 28, 2019 -

BOSTON & PHILADELPHIA--(BUSINESS WIRE)--May 3, 2019-- [Alexion Pharmaceuticals, Inc.](#) (NASDAQ:ALXN) today announced that the *New England Journal of Medicine (NEJM)* published positive data from the Phase 3 PREVENT study of SOLIRIS® (eculizumab), a first-in-class complement inhibitor, in adult patients with anti-aquaporin-4 (AQP4) auto antibody-positive neuromyelitis optica spectrum disorder (NMOSD). NMOSD is a rare and devastating, autoimmune, inflammatory disorder of the central nervous system (CNS) characterized by sudden and unpredictable relapses, also known as attacks. Each relapse results in stepwise accumulation of disability, including blindness and paralysis and sometimes premature death. Uncontrolled complement activation triggered by anti-AQP4 auto antibodies is a major underlying mechanism of the disease.^{1,2,3} There is currently no approved therapy for patients with NMOSD. Today's [NEJM online publication](#) coincides with the American Academy of Neurology (AAN) Annual Meeting, May 4-10, 2019 in Philadelphia, where these data will also be presented in the [Emerging Science session](#) on May 7.

As [announced previously](#), 97.9 percent of patients receiving SOLIRIS were relapse-free at 48 weeks compared with 63.2 percent of patients receiving placebo. New data published in *NEJM* and to be presented for the first time at the AAN meeting confirm that the significant relapse reduction observed in the PREVENT study was sustained through three years of treatment. All patients receiving SOLIRIS monotherapy and the vast majority of patients receiving SOLIRIS in addition to immunosuppressive therapy (IST) were relapse-free. The safety profile of SOLIRIS was consistent with that seen in other clinical studies.

"Patients with NMOSD live in constant fear of an attack or relapse. In this devastating disease, where each relapse results in further disability, preventing relapses is the primary goal of treatment," said Sean Pittock, M.D., principal investigator of the PREVENT study, lead author of the *NEJM* article and director of Mayo Clinic's Center for Multiple Sclerosis and Autoimmune Neurology and Mayo's Neuroimmunology Laboratory in Rochester, Minnesota. "The results from the PREVENT study, the first placebo-controlled Phase 3 study in NMOSD, are groundbreaking and demonstrate that the vast majority of patients receiving eculizumab did not experience a relapse."

"The substantial reduction in relapse risk sustained through three years of SOLIRIS treatment was consistent across all patients, regardless of their baseline immunosuppressive therapy use," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "These results provide hope for a promising new way of treating patients with NMOSD, who currently have no approved treatment options."

Proportion of relapse-free patients over time* in the PREVENT study, based on the primary endpoint of time to first adjudicated on-trial relapse, as published in *NEJM* and presented at AAN

Patients treated (n at baseline [0 weeks])	Proportion of relapse-free patients [%]		
	48 weeks (n)	96 weeks (n)	144 weeks (n)
All patients (100%)[†]			
SOLIRIS (96)	97.9 (68)	96.4 (46)	96.4 (22)
Placebo (47)	63.2 (21)	51.9 (9)	45.4 (4)
Patients receiving concomitant supportive IST (76.2%)[‡]			
SOLIRIS (75)	97.3 (54)	95.4 (35)	95.4 (13)
Placebo (34)	64.3 (17)	55.0 (7)	55.0 (3)
Patients not receiving concomitant supportive IST (23.8%)[‡]			
SOLIRIS (21)	100.0 (14)	100.0 (11)	100.0 (9)
Placebo (13)	60.6 (4)	40.4 (2)	20.2 (1)

p-values from log-rank tests are all <0.0001.

IST: Immunosuppressive therapy

* Based on the Kaplan-Meier product limit method.

† Primary endpoint

‡ Summaries for subgroups with different concomitant supportive IST were pre-specified. Statistical testing was post-hoc. In this summary, the individual concomitant supportive IST subgroups were combined.

The most common adverse events observed in the PREVENT study were upper respiratory tract infection (29% of patients in the SOLIRIS group vs. 13% in the placebo group), headache (23 vs. 23%), nasopharyngitis (21 vs. 19%), and nausea (17 vs. 26%). The serious adverse events that were reported for more than one patient in either group were pneumonia (three patients in the SOLIRIS group vs. one patient in the placebo group) and cellulitis, sepsis and urinary tract infection (two patients for each event in the SOLIRIS group vs. no patient in the placebo group). One patient receiving SOLIRIS and concomitant supportive IST died from infectious pleural effusion. The patient had an extensive history of pulmonary disease and was an active smoker. No cases of meningococcal infection were observed in the study.

The U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) are reviewing Alexion's applications for approval of SOLIRIS as a treatment for patients with NMOSD who are anti-AQP4 antibody-positive. The FDA granted [priority review](#) and set a Prescription Drug User Fee Act (PDUFA) action date of June 28, 2019.

About the PREVENT Study

The Prevention of Relapses and Evaluation of Eculizumab in NMOSD Treatment (PREVENT) study was a multinational (70 sites in 18 countries), 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 were required 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 NMOSD relapses. Patients were allowed to receive stable maintenance doses of protocol permitted supportive immune suppressive therapies (ISTs) for relapse prevention. Almost 25 percent of patients did not receive ISTs during the study. Patients were vaccinated against *Neisseria meningitidis* before receiving study treatment.

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 assignment. Adjudication decisions were based on objective and consistent clinical criteria described in a relapse adjudication charter. 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 open-label extension study to receive SOLIRIS. One hundred and nineteen patients entered the extension study.

About NMOSD

Neuromyelitis optica spectrum disorder (NMOSD) is a rare and devastating, autoimmune, inflammatory disorder of the central nervous system (CNS), typically involving the optic nerves and spinal cord. Patients experience an unpredictable, relapsing, and deteriorating course of disease with each attack, or relapse adding to their disability, and potentially leading to premature death.^{1,2,3,4} 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.^{3,5,6} One third (34%) of patients sustain permanent motor disability, almost one quarter (23%) become wheelchair-dependent, almost one fifth (18%) suffer from permanent visual disability, and almost one in 10 (9%) die.⁷ The disease primarily affects women.⁸ There is currently no approved therapy for patients with NMOSD.

In patients with NMOSD, uncontrolled complement activation triggered by auto-antibodies against anti-aquaporin-4 (AQP4), a water channel protein present on certain cells (astrocytes) in the CNS, results in the destruction of these cells, an increased permeability of the blood brain barrier, the destruction of cells (oligodendrocytes) surrounding nerve cells, the damage of the covering of nerve cells (demyelination) and ultimately the death of these nerve cells, predominantly in the optic nerves and spinal cord. This damage causes the relapses, which can ultimately result in blindness, paralysis and sometimes death.^{9,10,11,12,13} Patients with AQP4 auto antibodies represent approximately three quarters of all patients with NMOSD.^{14,15,16,17}

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. The terminal complement cascade, 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), anti-acetylcholine receptor (AChR) antibody-positive myasthenia gravis (MG), and anti-aquaporin-4 (AQP4) antibody-positive neuromyelitis optica spectrum disorder (NMOSD). SOLIRIS is approved in the U.S., EU, Japan and other countries as a treatment for adult patients with PNH and for adults and children with aHUS. SOLIRIS is not indicated for the treatment of patients with Shiga-toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS). In the U.S., SOLIRIS is also approved for the treatment of adult patients with generalized MG (gMG) who are anti-AChR antibody-positive, in the EU as the first and only approved treatment of refractory gMG in adults 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 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 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).

Dr. Pittock reports grants, personal fees and nonfinancial support from Alexion; grants from Grifols S.A. and Autoimmune Encephalitis Alliance; and grants, personal fees, nonfinancial and other support from Viela Bio. Dr. Pittock has patent No. 9,891,219 (application No. 12-573942), "Methods for Treating Neuromyelitis Optica by Administration of Eculizumab to an Individual That Is Aquaporin-4 (AQP4)-IgG Autoantibody Positive."

U.S. Indication for SOLIRIS® (eculizumab)

SOLIRIS is a prescription medicine called a monoclonal antibody. SOLIRIS is used to treat patients with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH), adults and children with a disease called atypical Hemolytic Uremic Syndrome (aHUS) (SOLIRIS is not for use in treating people with Shiga toxin *E. coli* related hemolytic uremic syndrome [STEC-HUS]), and adults with a disease called generalized Myasthenia Gravis

(gMG) who are anti-acetylcholine receptor (AChR) antibody positive. It is not known if SOLIRIS is safe and effective in children with PNH or gMG.

U.S. Important Safety Information for SOLIRIS® (eculizumab)

SOLIRIS is a medicine that affects the immune system. SOLIRIS can lower the ability of the immune system to fight infections. SOLIRIS increases the chance of getting serious and life-threatening meningococcal infections. Meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

Meningococcal vaccines must be received at least 2 weeks before the first dose of SOLIRIS if one has not already had this vaccine. If one's doctor decided that urgent treatment with SOLIRIS is needed, meningococcal vaccination should be administered as soon as possible. If one has not been vaccinated and SOLIRIS therapy must be initiated immediately, 2 weeks of antibiotics should also be administered with the vaccinations. If one had a meningococcal vaccine in the past, additional vaccination might be needed before starting SOLIRIS. Call one's doctor or get emergency medical care right away if any of these signs and symptoms of a meningococcal infection occur: headache with nausea or vomiting, headache and fever, headache with a stiff neck or stiff back, fever, fever and a rash, confusion, muscle aches with flu-like symptoms, and eyes sensitive to light.

SOLIRIS is only available through a program called the [SOLIRIS REMS](#).

SOLIRIS may also increase the risk of other types of serious infections. If one's child is treated with SOLIRIS, make sure that the child receives vaccinations against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). Certain people may be at risk of serious infections with gonorrhea. Talk to the doctor about whether one is at risk for gonorrhea infection, about gonorrhea prevention, and regular testing. Certain fungal infections (Aspergillus) may also happen if one takes SOLIRIS and has a weak immune system or a low white blood cell count.

Before one receives SOLIRIS, tell the doctor about all of the medical conditions, including if one: has an infection or fever, is pregnant or plans to become pregnant, and is breastfeeding or plans to breastfeed. It is not known if SOLIRIS will harm an unborn baby. It is not known if SOLIRIS passes into the breast milk.

Tell the doctor about all the medicines one takes, including prescription and over-the-counter medicines, vitamins, and herbal supplements. SOLIRIS and other medicines can affect each other causing side effects.

It is important that one: has all recommended vaccinations before starting SOLIRIS, receives 2 weeks of antibiotics if one immediately starts SOLIRIS, and stays up-to-date with all recommended vaccinations during treatment with SOLIRIS. Know the medications one takes and the vaccines one receives. Keep a list of them to show the doctor and pharmacist when one gets a new medicine.

If one has PNH, the doctor will need to monitor closely for at least 8 weeks after stopping SOLIRIS. Stopping treatment with SOLIRIS may cause breakdown of the red blood cells due to PNH. Symptoms or problems that can happen due to red blood cell breakdown include: drop in the number of the red blood cell count, drop in the platelet counts, confusion, kidney problems, blood clots, difficulty breathing, and chest pain.

If one has aHUS, the doctor will need to monitor closely for at least 12 weeks after stopping SOLIRIS for signs of worsening aHUS symptoms or problems related to abnormal clotting (thrombotic microangiopathy). Symptoms or problems that can happen with abnormal clotting may include: stroke, confusion, seizure, chest pain (angina), difficulty breathing, kidney problems, swellings in arms or legs and a drop in platelet count.

SOLIRIS can cause serious side effects including serious allergic reactions. Serious allergic reactions can happen during one's SOLIRIS infusion. Tell the doctor or nurse right away if one gets any of these symptoms during the SOLIRIS infusion: chest pain, trouble breathing or shortness of breath, swelling of the face, tongue, or throat, and feeling faint or pass out. If one has an allergic reaction to SOLIRIS, the doctor may need to infuse SOLIRIS more slowly, or stop SOLIRIS. The most common side effects in people with PNH treated with SOLIRIS include: headache, pain or swelling of the nose or throat (nasopharyngitis), back pain, and nausea. The most common side effects in people with aHUS treated with SOLIRIS include: headache, diarrhea, high blood pressure (hypertension), common cold (upper respiratory infection), stomach-area (abdominal pain), vomiting, pain or swelling of the nose or throat (nasopharyngitis), low red blood cell count (anemia), cough, swelling of legs or feet (peripheral edema), nausea, urinary tract infections, and fever. The most common side effects in people with gMG treated with SOLIRIS include: muscle and joint (musculoskeletal) pain.

Please see the accompanying full U.S. [Prescribing Information](#) and [Medication Guide](#) for SOLIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections, also available at: www.soliris.net.

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 commercialized two approved complement inhibitors to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) as well as the first and only approved complement inhibitor to treat atypical hemolytic uremic syndrome (aHUS) and anti-acetylcholine receptor (AChR) antibody-positive generalized myasthenia gravis (gMG), and is also developing it for patients with neuromyelitis optica spectrum disorder (NMOSD). 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 several mid-to-late-stage therapies, including a second complement inhibitor, a copper-binding agent for Wilson disease and an anti-neonatal Fc receptor (FcRn) antibody for rare Immunoglobulin G (IgG)-mediated diseases as well as several early-stage therapies, including one for light chain (AL) amyloidosis and a second anti-FcRn therapy. 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.

[ALXN-G]

Forward-Looking Statement

This press release contains forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Alexion, including statements related to: preventing relapses is the primary goal of NMOSD treatment; the results of Phase 3 PREVENT study of SOLIRIS® in adult patients with anti-aquaporin-4 (AQP4) auto antibody-positive NMOSD provide hope for a promising new way of treating patients with NMOSD; the impact that the relapse reduction could have for patients with NMOSD using SOLIRIS; SOLIRIS may be a promising new treatment for NMOSD; and future plans to present additional results and findings from Phase 3 of the PREVENT Study. 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 anticipated benefits of SOLIRIS as a treatment for NMOSD may not be realized; 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 failure to receive (or meaning delay in receipt of) regulatory approval for SOLIRIS as a treatment for NMOSD; the failure to deliver additional information at conferences regarding clinical trials; 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 March 31, 2019 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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