FDA Grants Priority Review and Accepts sBLA of SOLIRIS® (Eculizumab) as a Treatment for Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD)

February 22, 2019

FDA sets action date of June 28, 2019

Filing in the European Union under review, and filing in Japan planned for Q1 2019

BOSTON--(BUSINESS WIRE)--Feb. 22, 2019-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced that the U.S. Food and Drug Administration (FDA) has accepted for review a supplemental Biologics License Application (sBLA) for the use of SOLIRIS® (eculizumab), the company's first C5 complement inhibitor, as a treatment for patients with neuromyelitis optica spectrum disorder (NMOSD) who have anti-aquaporin-4 (AQP4) auto antibodies. The FDA granted priority review and set a Prescription Drug User Fee Act (PDUFA) action date of June 28, 2019. The application is supported by comprehensive data from the successful PREVENT study in patients with anti-AQP4 auto antibody-positive NMOSD.

"Given the debilitating impact NMOSD relapses can have on patients and the fact that there is currently no approved therapy, we are committed to getting SOLIRIS to these patients as quickly as possible," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "Based on our strong clinical data, we believe that SOLIRIS can provide significant therapeutic benefits, and we look forward to working with the FDA to facilitate a rapid review."

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]

The European Medicines Agency (EMA) is reviewing Alexion's application to add the treatment of NMOSD to the marketing authorization for SOLIRIS in the European Union (EU), submitted in January 2019. In addition, Alexion is preparing to submit a supplemental New Drug Application for SOLIRIS in NMOSD in Japan in Q1 2019. SOLIRIS has received Orphan Drug Designation (ODD) for the treatment of patients with NMOSD in the U.S., EU and Japan.

About NMOSD

NMOSD is a rare and 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] Anti-AQP4 auto-antibody testing is available for the diagnosis of NMOSD. The disease primarily affects women, often in the prime of their lives.[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 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. When activated in an uncontrolled manner, complement 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) auto antibody-positive neuromyelitis optica spectrum disorder (NMOSD). SOLIRIS is approved in the U.S., EU, Japan and other countries as a treatment for patients with PNH and aHUS, in the U.S. for the treatment of adult patients with generalized MG (gMG) who are anti-AchR antibody-positive, in the EU as the first and only 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 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) as a treatment for patients with PNH in the U.S., EU, Japan and many other countries, as a treatment for patients with aHUS in the U.S., EU, and many other countries, as a treatment for patients with MG in the U.S. and EU, as a treatment for patients with refractory gMG in Japan and as a treatment for 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
SOLIRIS is a prescription medicine called a monoclonal antibody. SOLIRIS is used to treat patients with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH). It is not known if SOLIRIS is safe and effective in children with PNH.

SOLIRIS is a medicine that affects the immune system. SOLIRIS can lower the ability of your immune system to fight infections. SOLIRIS increases your 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.

You must receive meningococcal vaccines at least 2 weeks before your first dose of SOLIRIS if you have not already had this vaccine. If your doctor decided that urgent treatment with SOLIRIS is needed, you should receive meningococcal vaccination as soon as possible. If you have not been vaccinated and SOLIRIS therapy must be initiated immediately, you should also receive 2 weeks of antibiotics with your vaccinations. If you had a meningococcal vaccine in the past, you might need additional vaccination before starting SOLIRIS. Call your doctor or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection: 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 your child is treated with SOLIRIS, make sure that your 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 your doctor about whether you are at risk for gonorrhea infection, about gonorrhea prevention, and regular testing. Certain fungal infections (Aspergillus) may also happen if you take SOLIRIS and have a weak immune system or a low white blood cell count.

Before you receive SOLIRIS, tell your doctor about all of your medical conditions, including if you: have an infection or fever, are pregnant or plan to become pregnant. It is not known if SOLIRIS will harm your unborn baby, or are breastfeeding or plan to breastfeed. It is not known if SOLIRIS passes into your breast milk.

Tell your doctor about all the medicines you take, 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 you: have all recommended vaccinations before you start SOLIRIS, receive 2 weeks of antibiotics if you immediately start SOLIRIS, and stay up-to-date with all recommended vaccinations during treatment with SOLIRIS. Know the medications you take and the vaccines you receive. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

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

SOLIRIS can cause serious side effects including serious allergic reactions. Serious allergic reactions can happen during your SOLIRIS infusion. Tell your doctor or nurse right away if you get any of these symptoms during your SOLIRIS infusion: chest pain, trouble breathing or shortness of breath, swelling of your face, tongue, or throat, and feel faint or pass out. If you have an allergic reaction to SOLIRIS, your 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 your nose or throat (nasopharyngitis), back pain, and nausea.

Please see the accompanying full Prescribing Information and Medication Guide for SOLIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections, 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 commercializes 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. 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, including statements related to: planned submission of regulatory applications for review and approval by regulatory authorities in Japan for SOLIRIS® as a treatment for patients with neuromyelitis optica spectrum disorder (NMOSD) (and the timing of such submission); the Company's commitment to getting SOLIRIS to NMOSD patients as quickly as possible; the Company's future plans to work with the FDA to facilitate a rapid review of the supplemental Biologics License Application (sBLA) submission for SOLIRIS as a treatment for NMOSD; SOLIRIS will be available in the future for use by patients with NMOSD; the impact that the relapse reduction could have for patients with NMOSD using SOLIRIS; and SOLIRIS may provide significant therapeutic benefits to patients with NMOSD. 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 patients with 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 Company's products may not provide the anticipated benefits to patients with certain indications (including NMOSD); future competition from biosimilars and novel products; the failure of regulatory agencies to approve use of the Company's products for use in indications included in the regulatory application; 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 patients with 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 patients with 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; failure to protect and enforce our data, intellectual property and proprietary rights and the risks and uncertainties relating to intellectual property claims, lawsuits and challenges against us; 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 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 Annual Report on Form 10-K for the year ended December 31, 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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