



## Alexion Announces Publication of Interim Data from Phase 3 Open-Label Extension Study Supporting Long-Term Efficacy and Safety of SOLIRIS® (Eculizumab) in Adult Patients with Generalized Myasthenia Gravis in Muscle & Nerve

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*-- New data suggest positive impact on clinical burden and sustained long-term clinical benefit for adult patients with anti-acetylcholine receptor (AChR) antibody-positive refractory generalized myasthenia gravis (gMG) --*

BOSTON--(BUSINESS WIRE)--Mar. 8, 2019-- [Alexion Pharmaceuticals, Inc.](#) (NASDAQ:ALXN) today announced the publication of data from an interim analysis of the Phase 3 open-label extension study (ECU-MG-302) of REGAIN (ECU-MG-301) evaluating the long-term efficacy and safety of SOLIRIS® (eculizumab) for the treatment of adult patients with anti-acetylcholine receptor (AChR) antibody-positive refractory generalized myasthenia gravis (gMG). Published in *Muscle & Nerve*, the results indicate that the improvements demonstrated during the initial six-month duration of the double-blinded Phase 3 REGAIN trial, were sustained over a treatment period of three years. Additionally, patients who had previously been treated with placebo in REGAIN showed rapid and significant improvement upon starting treatment with SOLIRIS in the open-label extension (OLE).

“Symptom persistence is a major challenge in the treatment of gMG,” said Srikanth Muppidi, M.D., Clinical Associate Professor, Department of Neurology and Neurosciences at Stanford University School of Medicine. “These results confirm that treatment with SOLIRIS can provide patients with anti-AChR antibody-positive gMG adult patients with tangible and durable clinical benefits and can help to reduce the burden of this devastating disease on patients and their families.”

At the time of data analysis more than 55% of patients enrolled in the OLE showed clinically meaningful response, based on the MG-Activities of Daily Living scale (MG-ADL), and the majority of patients (56%) achieved minimal manifestations or pharmacological remission.

The data from the OLE also confirm that the safety profile of SOLIRIS, when used to treat patients with anti-AChR antibody-positive gMG, is consistent with its safety profile seen in REGAIN. No cases of meningococcal infection were reported by the interim data cut-off [one case, which was resolved with antibiotic treatment, occurred after this date], and the most common adverse events were headache (37.6% of patients) and nasopharyngitis (31.6%). The most common serious adverse event was myasthenia gravis worsening (12.8% of patients). When compared with data from the year prior to the start of REGAIN, patients in the OLE experienced significant reductions in rates of exacerbations (75% reduction) and hospitalization (83% reduction).

Data reported in this interim analysis were based on results from 117 patients who received SOLIRIS (1,200 mg, every 2 weeks) for a median duration of almost two years (22.7 months). Patients enrolled in the OLE received SOLIRIS for a maximum of four years. Symptom improvement was evaluated with multiple assessment tools, including the MG-ADL, the Quantitative MG scale (QMG), the MG Composite scale (MGC) and the 15-item MG Quality of Life questionnaire (MG-QOL 15).

“As the first FDA-approved treatment for gMG in more than 60 years, SOLIRIS represents an important option for adult patients with anti-AChR antibody-positive gMG who previously experienced persistent symptoms and significant morbidities despite previous therapy,” said José Menoyo, M.D., Vice President, U.S. Medical Affairs at Alexion. “We hope that this analysis of our open-label extension study contributes to the overall understanding of the burden of disease and provides confidence in the safety and benefit of long-term SOLIRIS treatment for this population.”

### **About the Open-Label Extension Study (ECU-MG-302)**

94% (117/125) of patients who completed the REGAIN study enrolled in the open-label extension, of which 56 continued to receive SOLIRIS (SOLIRIS/SOLIRIS group) and 61 were switched from placebo to SOLIRIS (placebo/SOLIRIS group) within two weeks of completing the REGAIN study. Patients were not informed of prior treatment assignment in REGAIN through a four-week blinded induction phase, after which all patients received ongoing open-label treatment with SOLIRIS (1,200 mg/dose) every two weeks. For this interim analysis, 49 patients in the SOLIRIS/SOLIRIS group and 56 patients in the placebo/SOLIRIS group completed week 26 assessments; 49 patients in the SOLIRIS/SOLIRIS group and 54 patients in the placebo/SOLIRIS group completed week 52 assessments; and 47 patients in the SOLIRIS/SOLIRIS group and 49 patients in the placebo/SOLIRIS group completed week 78 assessments. Mean scores over time were calculated using repeated measures from baseline. The study was completed in January 2019.

### **About REGAIN (ECU-MG-301)**

This was a randomized, double-blind, placebo-controlled, multicenter Phase 3 clinical study that evaluated the efficacy and safety of SOLIRIS over 26 weeks in 125 patients with a confirmed diagnosis of refractory gMG with positive serologic test for antibodies against AChR. Patients initially received 900 mg of SOLIRIS or placebo weekly for 4 weeks followed by 1,200 mg of SOLIRIS or placebo 1 week later, and then 1,200 mg of SOLIRIS or placebo every 2 weeks. The primary efficacy endpoint of change from baseline in MG-ADL total score at week 26, as well as the three secondary endpoints —changes from baseline in QMG, MGC, and MG-QOL 15—were assessed using a worst-rank analysis.

The REGAIN study (ECU-MG-301) and its open-label extension study (ECU-MG-302) are sponsored by Alexion.

### **About Generalized Myasthenia Gravis**

Myasthenia gravis (MG) is a debilitating, chronic and progressive autoimmune neuromuscular disease that can occur at any age but most commonly begins for women before the age of 40 and men after the age of 60.<sup>1-4</sup> It typically begins with weakness in the muscles that control the movements of the eyes and eyelids, and often progresses to the more severe and generalized form, known as gMG, with weakness of the head, neck, trunk, limb and respiratory muscles.<sup>4</sup>

While most patients with gMG can be managed with current therapies for MG, 10-15% of patients fail to respond adequately to or cannot tolerate multiple therapies for MG and continue to suffer profound muscle weakness, and severe disease symptoms that limit function.<sup>5,6,7</sup> These patients can suffer from slurred speech, choking, impaired swallowing, double or blurred vision, disabling fatigue, immobility requiring assistance, shortness of breath, and episodes of respiratory failure. Complications, exacerbations and myasthenic crises can require hospital and intensive care unit admissions with prolonged stays and can be life-threatening.<sup>2,3,8</sup>

In patients with anti-AChR antibody-positive MG, the body's own immune system turns on itself to produce antibodies against AChR, a receptor located on muscle cells at the neuromuscular junction (NMJ) and used by nerve cells to communicate with the muscles these nerves control.<sup>2,3</sup> The binding of these antibodies to AChR activates the complement cascade, another part of the immune system, which leads to a localized inflammation and destruction of the muscle membrane at the NMJ.<sup>9-11</sup> As a result, the communication between nerve and muscle is impaired, which in turn leads to a loss of normal muscle function.<sup>2,3</sup>

Patients with anti-AChR antibody-positive gMG who continue to suffer from severe disease symptoms and complications despite current therapies for MG represent approximately 5-10% of all patients with MG.<sup>1-4</sup>

#### **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 generalized myasthenia gravis (gMG). 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. 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 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 infections, available at [www.soliris.net](http://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). SOLIRIS is also used to treat 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). SOLIRIS is also approved to treat 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.

SOLIRIS is a medicine that affects the immune system. SOLIRIS can lower the ability of your 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 your platelet counts, confusion, kidney problems, blood clots, difficulty breathing, and chest pain.

If one has aHUS, the doctor will need to monitor closely during and for at least 12 weeks after stopping treatment 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, a drop in the 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 feel 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; fever. The most common side effects in people with gMG treated with SOLIRIS include: muscle and joint (musculoskeletal) pain.

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](http://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 anti-aquaporin-4 (AQP4) auto antibody-positive 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](http://www.alexion.com).

#### **References:**

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