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## **Alexion Initiates Multinational Registration Trials of Eculizumab as a Potential Treatment for Patients with Relapsing Neuromyelitis Optica (NMO) and Refractory Generalized Myasthenia Gravis (MG)**

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals (Nasdaq:ALXN) today announced the initiation of a single, multinational, placebo-controlled trial to evaluate the safety and efficacy of eculizumab (Soliris®) in patients with relapsing neuromyelitis optica (NMO), a life-threatening, ultra-rare neurologic disorder. Alexion also initiated a single, multinational, placebo-controlled trial in patients with refractory generalized myasthenia gravis (MG), another rare and debilitating neurologic disorder.

Both NMO and MG are disorders caused by uncontrolled complement activation. In patients with NMO, chronic, uncontrolled complement activation results in severe damage to the central nervous system (CNS), predominantly impacting the optic nerve and spinal cord. This devastating disease is characterized by severe weakness, paralysis, respiratory failure, loss of bowel and bladder function, blindness and premature death. Currently, there are no approved treatments for NMO. In patients with MG, uncontrolled complement activation due to antibodies directed at the neuromuscular junction can ultimately lead to profound and debilitating weakness of various muscle groups throughout the body. Patients with generalized MG develop significant muscle weakness, impairing their ability to walk, speak clearly, swallow and, in some cases, to breathe normally.

"Since complement activation plays a pivotal role in the pathophysiology of both NMO and MG, the mechanism of action of eculizumab, as a terminal complement inhibitor, suggests it may have the potential to help patients living with these rare and devastating disorders," said Martin Mackay, Ph.D., executive vice president and global head of R&D at Alexion. "We look forward to enrolling patients in these placebo-controlled studies to confirm the clinical benefits of eculizumab in the treatment of NMO and MG, which would be an important development for these underserved patient populations."

Soliris is currently approved in the United States, European Union, Japan and other countries for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is not approved in any country for the treatment of NMO or MG.

### **About The NMO Study**

The trial is a multinational, double-blind, placebo-controlled study with the primary objective of assessing the efficacy of eculizumab compared to placebo in patients with relapsing NMO, based on the time to first relapse and relapse risk reduction. Secondary endpoints include safety and tolerability as well as additional efficacy outcome measures. Patient enrollment and dosing have commenced in this trial. Recruitment is open to adults with a diagnosis of NMO or NMO spectrum disorder with relapsing disease. More information about the NMO trial is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) under the identifier NCT01892345.

This trial is based on results from an investigator-initiated study which was recently published in the *Lancet Neurology* journal. In that study, treatment with eculizumab was associated with a significant reduction in the frequency of relapses (recurring attacks) in patients with severe, relapsing NMO.<sup>1</sup>

In June 2013 the U.S. Food and Drug Administration (FDA) granted eculizumab an orphan drug designation for the treatment of NMO. Eculizumab was also granted orphan medicinal product designation from the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA) for the treatment of NMO in August 2013.

### **About The MG Study**

The trial is a multinational, double-blind, parallel-group, placebo-controlled study with the primary objective to assess the efficacy of eculizumab compared to placebo on patients' motor function, as measured by the improvement in MG- Activities of Daily Living (MG-ADL) score at 26 weeks. Secondary endpoints include safety and tolerability as well as additional efficacy measures. Patient screening has commenced in this study. Recruitment is open to adults with a diagnosis of refractory generalized MG, with an MG-ADL total score of at least 6 demonstrating continued muscle weakness despite treatment. More information about the MG trial is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) under the identifier NCT01997229.

This trial is based on preliminary evidence from a Company-sponsored Phase 2 pilot study in a small group of 14 patients that evaluated the safety and efficacy of eculizumab in the treatment of refractory generalized MG.<sup>2</sup> In the pilot study, 86% (6/7) of

patients receiving a 16-week course of eculizumab therapy achieved at least a 3-point reduction in the total Quantitative Myasthenia Gravis (QMG) score, compared to 57% (4/7) of patients treated with placebo. Similarly, 86% (6/7) of patients in the eculizumab arm had at least a 2-point improvement in MG-ADL, compared to 57% (4/7) in the placebo arm; the mean change in MG-ADL was -4.1 points in the eculizumab-treated patients. Since a 2-point change in MG-ADL is considered clinically meaningful,<sup>3</sup> the 4.1-point change in the pilot study suggests a robust treatment effect. Eculizumab therapy was well tolerated in the study.<sup>2</sup>

### **About Neuromyelitis Optica (NMO)**

In patients with neuromyelitis optica (NMO), binding of NMO-IgG antibody to astrocytes results in uncontrolled complement activation and destruction of myelin-producing cells, leading to severe damage to the central nervous system and predominantly impacting the spinal cord and optic nerve.<sup>4-6</sup> The disease is characterized by severe weakness, paralysis, respiratory failure, loss of bowel and bladder function, blindness and premature death.<sup>7-9</sup> Patients with NMO have a life-long exposure to the uncontrolled terminal complement activation due to chronic autoimmune attack, and most patients experience an unpredictable, relapsing course of disease with cumulative disability, as each attack adds to the neurologic disability.<sup>8,10,11</sup> Fifty percent of relapsing NMO patients have been reported to sustain permanent severe disability, including paralysis and blindness, within five years of disease onset.<sup>12</sup> Most NMO-related deaths result from respiratory complications from NMO attacks.<sup>12,13</sup> The disease primarily affects women, with a female to male ratio as high as a 9:1.<sup>14</sup> Currently, there are no approved treatments for NMO.

### **About Myasthenia Gravis (MG)**

Myasthenia gravis (MG) is a rare, debilitating neurologic disorder caused by auto-antibodies that recognize a specific target in the nerve-muscle junction, which results in life-long uncontrolled terminal complement activation causing tissue damage and interference with signaling between nerve and muscle fibers.<sup>15,16</sup> Patients with MG initially experience weakness in their ocular (eye) muscles, and the disease typically progresses to the more severe and generalized form to include weakness of head, trunk, limb and respiratory muscles. Symptoms can include drooping eyelid, weakness in the arms and legs, slurred speech, difficulty chewing or swallowing, and difficulty breathing.

### **About Soliris® (eculizumab)**

Soliris® (eculizumab) is a first-in-class terminal complement inhibitor developed from the laboratory through regulatory approval and commercialization by Alexion. Soliris is approved in the U.S. (2007), European Union (2007), Japan (2010) and other countries as the first and only treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH), a debilitating, ultra-rare and life-threatening blood disorder, characterized by complement-mediated hemolysis (destruction of red blood cells). Soliris is indicated to reduce hemolysis. Soliris is also approved in the U.S. (2011), the European Union (2011), Japan (2013) and other countries as the first and only treatment for patients with atypical hemolytic uremic syndrome (aHUS), a debilitating, ultra-rare and life-threatening genetic disorder characterized by complement-mediated thrombotic microangiopathy, or TMA (blood clots in small vessels). Soliris is not approved for the treatment of NMO or MG in any country.

Alexion's breakthrough approach in terminal complement inhibition has received the pharmaceutical industry's highest honors: the 2008 Prix Galien USA Award for Best Biotechnology Product with broad implications for future biomedical research and the 2009 Prix Galien France Award in the category of Drugs for Rare Diseases. More information, including the full prescribing information on Soliris, is available at [www.soliris.net](http://www.soliris.net).

### **Important Safety Information**

The U.S. product label for Soliris includes a boxed warning: "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 Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies. Immunize patients with a meningococcal vaccine 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. (See Serious Meningococcal Infections (5.1) for additional guidance on the management of 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)."

In patients with PNH, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, nasopharyngitis (runny nose), back pain and nausea. 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. In patients with aHUS, the most frequently reported adverse events observed with Soliris treatment in clinical studies were hypertension, upper respiratory tract infection, diarrhea, headache, anemia, vomiting, nausea, urinary tract infection, and leukopenia. Please see full prescribing information for Soliris, including boxed WARNING regarding risk of serious meningococcal infection.

## About Alexion

Alexion is a biopharmaceutical company focused on serving patients with severe and rare disorders through the innovation, development and commercialization of life-transforming therapeutic products. Alexion is the global leader in complement inhibition and has developed and markets Soliris<sup>®</sup> (eculizumab) as a treatment for patients with PNH and aHUS, two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is currently approved in nearly 50 countries for the treatment of PNH, and in the United States, European Union, Japan and other countries for the treatment of aHUS. Alexion is evaluating other potential indications for Soliris in additional severe and ultra-rare disorders beyond PNH and aHUS, and is developing other highly innovative biotechnology product candidates across multiple therapeutic areas. This press release and further information about Alexion can be found at: [www.alexionpharma.com](http://www.alexionpharma.com).

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## Safe Harbor Statement

*This news release contains forward-looking statements, including statements related to potential medical benefits of Soliris<sup>®</sup> (eculizumab) for the treatment of neuromyelitis optica (NMO) and myasthenia gravis (MG). 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 marketing approval or material limitations on the marketing of Soliris for NMO or MG, delays in arranging satisfactory manufacturing capabilities, the possibility that results of clinical trials are not predictive of safety and efficacy results of Soliris for NMO or MG in broader or different patient populations, decisions of regulatory authorities to require additional testing, the risk that estimates regarding the number of patients with NMO or MG and observations regarding the natural history of patients with NMO or MG are inaccurate, and a variety of other risks set forth from time to time in Alexion's filings with the Securities and Exchange Commission, including but not limited to the risks discussed in Alexion's Annual Report on Form 10-K for the period ended Dec. 31, 2013. 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.*

## References

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