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## Alexion Announces Topline Results from Phase 3 REGAIN Study of Eculizumab (Soliris®) in Patients with Refractory Generalized Myasthenia Gravis (gMG)

- Conference Call Scheduled for Today, June 6, 2016, at 5:00 p.m. ET-

- Detailed Results to be Presented at the 14<sup>th</sup> International Congress on Neuromuscular Diseases (ICNMD) July 7 in Toronto-

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ: ALXN) today announced topline results from the REGAIN study, a Phase 3 registration trial of eculizumab (Soliris®) in patients with refractory generalized myasthenia gravis (gMG). Refractory gMG is an ultra-rare segment of MG—a debilitating, complement-mediated neuromuscular disease—in which patients have largely exhausted conventional therapy and continue to suffer profound muscle weakness throughout the body, resulting in slurred speech, impaired swallowing and choking, double vision, upper and lower extremity weakness, disabling fatigue, shortness of breath due to respiratory muscle weakness, and episodes of respiratory failure.<sup>1-5</sup> In the study, the primary efficacy endpoint of change from baseline in Myasthenia Gravis-Activities of Daily Living Profile (MG-ADL) total score, a patient-reported assessment, at week 26, did not reach statistical significance ( $p=0.0698$ ) as measured by a worst-rank analysis.

The first prospectively defined secondary efficacy endpoint of change from baseline in Quantitative Myasthenia Gravis (QMG) total score, a physician-administered assessment of MG clinical severity, with eculizumab treatment compared to placebo at week 26, achieved a p-value of 0.0129 as measured by a worst-rank analysis. In addition, the second and third prospectively defined secondary efficacy endpoints of responder status in MG-ADL and QMG achieved p-values  $< 0.05$ : the proportion of patients with at least a 3-point reduction in MG-ADL total score and no rescue therapy from baseline to week 26 with eculizumab treatment compared to placebo achieved a p-value of 0.0229, and the proportion of patients with at least a 5-point reduction in QMG total score and no rescue therapy from baseline to week 26 with eculizumab treatment compared to placebo achieved a p-value of 0.0018.

"While the REGAIN study missed its primary endpoint, I am encouraged by the clinically meaningful improvements in MG-ADL and QMG measures in patients treated with eculizumab compared with placebo. The magnitude of effect on QMG observed in this large, prospective registration trial is unprecedented in my more than 30 years of clinical investigation of refractory MG patients, and I look forward to presenting additional outcomes at ICNMD," said James F. Howard Jr., M.D., Distinguished Professor of Neuromuscular Disease, Professor of Neurology, Medicine & Allied Health, and Chief, Neuromuscular Disorders Section, The University of North Carolina School of Medicine. "There is an urgent need in the MG community for a therapy with the potential to dramatically improve the lives of patients with refractory MG, who continue to experience profound complement-mediated muscle weakness that makes it difficult or impossible to perform simple daily activities, including walking, talking, swallowing, and even breathing normally."

Pre-specified sensitivity analyses were prospectively defined to validate results for the primary and first secondary endpoints. Three of the four prospectively defined sensitivity analyses around the primary endpoint of MG-ADL achieved p-values  $< 0.05$ , including the sensitivity analysis for change from baseline in MG-ADL using repeated measures, which showed a mean change with eculizumab treatment at week 26 of -4.2 versus a mean change with placebo at week 26 of -2.3 and achieved a p-value of 0.0058. Additionally, all four prospectively defined sensitivity analyses around the first secondary endpoint of QMG achieved p-values  $< 0.05$ , including the sensitivity analysis for change from baseline in QMG using repeated measures, which showed a mean change with eculizumab treatment at week 26 of -4.6 versus a mean change with placebo at week 26 of -1.6 and achieved a p-value of 0.0006.

"The primary endpoint of the REGAIN study missed statistical significance, however the findings from this study underscore the pivotal role of complement inhibition in addressing the underlying pathophysiology of refractory gMG. Importantly, the totality of data reviewed to date, including the first three secondary endpoints and a series of prospectively defined sensitivity analyses, shows early and sustained substantial improvements over 26 weeks for patients treated with eculizumab compared to placebo," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "Today, patients with refractory gMG continue to suffer severe disease-related morbidities that often lead to hospital visits and ICU stays, despite currently available therapies. We look forward to discussing the results with regulators in the U.S. and Europe, and working together to address the urgent needs of patients with this devastating disease."

Alexion continues to analyze the data from the REGAIN study, and results will be presented on July 7, 2016, during the Hot

Topics session at the 14th International Congress on Neuromuscular Diseases (ICNMD) in Toronto.

The safety of eculizumab in this study was consistent with the Soliris labels. The most common adverse events in patients receiving eculizumab and placebo, respectively, were: headache (16.1%, 19.0%), upper respiratory tract infection (16.1%, 19.0%), nasopharyngitis (14.5%, 15.9%), myasthenia gravis (9.7%, 17.5%), and nausea (12.9%, 14.3%). Serious adverse events were reported in 14.5% of eculizumab patients and 28.6% of placebo patients. Four patients receiving eculizumab (6.5%) discontinued treatment due to an adverse event. There were no discontinuations due to adverse events in the placebo arm.

Ninety-four percent of patients (117 of 125) from the REGAIN study continued into a Phase 3 open-label extension study evaluating the safety and efficacy of eculizumab in the treatment of patients with refractory gMG. Eculizumab has received Orphan Drug Designation (ODD) for the treatment of patients with MG in the U.S., EU, and Japan. Eculizumab is not approved in any country for the treatment of patients with gMG.

### **REGAIN Study Design**

The REGAIN study is a randomized, double-blind, placebo-controlled, multicenter trial evaluating the safety and efficacy of eculizumab in patients with refractory gMG. The study enrolled and treated 125 adult patients across North America, South America, Europe, and Asia. Patients had a confirmed MG diagnosis with positive serologic test for anti-AChR antibodies. All patients were required to have previously failed treatment with at least two immunosuppressive agents or failed treatment with at least one immunosuppressive agent and required chronic plasma exchange or IVIg, and had an MG-ADL total score  $\geq 6$  at study entry.

Patients were randomized 1:1 to receive eculizumab or placebo for a total of 26 weeks. Patients initially received 900 mg of eculizumab or placebo weekly for 4 weeks followed by 1200 mg of eculizumab or placebo one week later, and then 1200 mg of eculizumab or placebo every two weeks. Patients were able to continue to receive stable dose and type of supportive immunosuppressive therapy (IST), but no new ISTs and no increase in IST dosage were permitted during the trial, unless patient required rescue therapy for disease worsening.

The primary efficacy endpoint of change from baseline in MG-ADL total score at week 26 and the first secondary endpoint of change from baseline in QMG total score at week 26 were assessed using a worst-rank score analysis.

### **Conference Call**

Alexion will host a conference call/webcast today, June 6, at 5:00 p.m. to discuss the data. To participate in this call, dial (844) 309-0617 (USA) or (661) 378-9464 (international), confirmation code 20710881, shortly before 5:00 p.m. A replay of the call will be available for a limited period following the call, beginning at 8:00 p.m. The replay number is (855) 859-2056 (USA) or (404) 537-3406 (international), confirmation code 20710881. The audio webcast can be found on the Investor page of Alexion's website at: <http://ir.alexionpharm.com>.

### **About Refractory Generalized Myasthenia Gravis**

Refractory generalized myasthenia gravis (gMG) is an ultra-rare segment of MG—a debilitating, complement-mediated neuromuscular disease—in which patients experience severe morbidities despite currently available MG therapies.<sup>1,2,3</sup>

MG typically begins with weakness in the ocular muscles and often progresses to the more severe and generalized form, known as gMG, to include weakness of the head, neck, trunk, limb and respiratory muscles.<sup>6</sup> While most gMG patients are managed with conventional therapies, 10% to 15% of patients are considered refractory—meaning they have largely exhausted conventional therapy and continue to suffer profound muscle weakness throughout the body, resulting in slurred speech, impaired swallowing and choking, double vision, upper and lower extremity weakness, disabling fatigue, shortness of breath due to respiratory muscle weakness, and episodes of respiratory failure.<sup>4,5,7</sup> Patients with refractory gMG frequently require hospitalization, often involving intensive care unit stays.<sup>8</sup>

Today, there are no therapies that are effective in this ultra-rare population of patients suffering from refractory gMG.

### **About Soliris® (eculizumab)**

Soliris 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) to reduce hemolysis. PNH is a debilitating, ultra-rare and life-threatening blood disorder, characterized by complement-mediated hemolysis

(destruction of red blood cells). Soliris is also approved in the U.S. (2011), European Union (2011), Japan (2013) and other countries as the first and only treatment for patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy, or TMA (blood clots in small vessels). aHUS is a debilitating, ultra-rare and life-threatening genetic disorder characterized by complement-mediated TMA. Soliris is not indicated for the treatment of patients with Shiga-toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS). For the breakthrough medical innovation in complement inhibition, Alexion and Soliris have received some of the pharmaceutical industry's highest honors: the Prix Galien USA (2008, Best Biotechnology Product) and France (2009, Rare Disease Treatment).

More information, including the full U.S. prescribing information, on Soliris is available at [www.soliris.net](http://www.soliris.net).

## About Alexion

Alexion is a global biopharmaceutical company focused on developing and delivering life-transforming therapies for patients with devastating and rare disorders. Alexion is the global leader in complement inhibition and has developed and commercialized the first and only approved complement inhibitor to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), two life-threatening ultra-rare disorders. In addition, Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). Alexion is advancing the most robust rare disease pipeline in the biotech industry with highly innovative product candidates in multiple therapeutic areas. This press release and further information about Alexion can be found at: [www.alexion.com](http://www.alexion.com).

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## Forward-Looking Statements

*This news release contains forward-looking statements, including statements related to the potential medical benefits and commercial potential of Soliris for the treatment of myasthenia gravis, and Alexion's future clinical, regulatory and commercial plans for Soliris for the treatment of myasthenia gravis. 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 our products, delays, interruptions or failures in the manufacture and supply of our products and our product candidates, progress in establishing and developing commercial infrastructure, failure to satisfactorily address matters raised by the FDA and other regulatory agencies, the possibility that results of clinical trials are not predictive of safety and efficacy results of our products in broader patient populations in the disease studied or other diseases, the possibility that clinical trials of our product candidates could be delayed or that additional research and testing is required by regulatory agencies, the adequacy of our pharmacovigilance and drug safety reporting processes, the risk that third party payors (including governmental agencies) will not reimburse or continue to reimburse for the use of our products at acceptable rates or at all, risks regarding government investigations, including the SEC and DOJ investigations, the risk that estimates regarding the number of patients with the diseases that our products treat are inaccurate, the risks of shifting foreign exchange rates, and a variety of other risks set forth from time to time in Alexion's filings with the U.S. Securities and Exchange Commission, including but not limited to the risks discussed in Alexion's Quarterly Report on Form 10-Q for the period ended March 31, 2016 and in our other filings with the U.S. Securities and Exchange Commission. 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.*

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