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## **Soliris® (Eculizumab) Receives Marketing Authorization in Japan for the Treatment of Patients with Generalized Myasthenia Gravis (gMG)**

*First and Only Approved Complement Inhibitor in Japan as a Treatment for Patients with gMG, a Chronic and Debilitating Neuromuscular Disorder*

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) announced today that the Ministry of Health, Labour and Welfare (MHLW) in Japan has approved Soliris® (eculizumab) as a treatment for patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive and whose symptoms are difficult to control with high-dose intravenous immunoglobulin (IVIG) therapy or plasmapheresis (PLEX). Soliris is the first and only complement inhibitor approved in Japan as a treatment for these patients. In the Phase 3 REGAIN study and its ongoing open-label extension study, Soliris demonstrated treatment benefits for patients with anti-AChR antibody-positive gMG who had previously failed immunosuppressive treatment and continued to suffer from significant unresolved disease symptoms, which can include difficulties seeing, walking, talking, swallowing and breathing.<sup>1,2,3</sup> These patients are at an increased risk of disease exacerbations and crises that may require hospitalization and intensive care and may be life-threatening.<sup>4,5</sup>

"Soliris represents an important treatment advance for patients in Japan with anti-AChR antibody-positive gMG who continue to suffer from significant unresolved disease symptoms despite existing treatment options," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "We are proud that these patients will be able to benefit from our deep understanding of complement biology, which allowed us to develop Soliris as treatment for this debilitating neuromuscular disorder."

Chronic uncontrolled activation of the complement system, a part of the immune system, plays a major role in the debilitating symptoms and potentially life-threatening complications for patients with gMG who are anti-AChR antibody-positive.<sup>6,7,8</sup> By selectively and effectively inhibiting the terminal complement cascade, Soliris targets a critical underlying cause of the disease.

"It is exciting that patients with gMG in Japan whose symptoms are difficult to control will now have a new treatment option," said Professor and Chairman Hiroyuki Murai, M.D., Ph.D., Department of Neurology at the International University of Health and Welfare, School of Medicine, Tokyo, Japan and an investigator in the clinical development of this new indication. "I am pleased that the Ministry appreciated the ability of Soliris to improve patients' symptoms, their ability to carry out activities of daily living and their quality of life."

"This approval is great news for patients with gMG in Japan who fail to adequately respond to existing therapies and continue to face significant disease symptoms," said Michiyo Sakurai, President of the Japanese Myasthenia Gravis Association, Kyoto, Japan. "The inability to carry out activities of daily living can be very debilitating and frustrating for these patients and their families and friends. They welcome this new therapy option and the hope that it provides to them."

Japan's MHLW based its approval of this new indication of Soliris on comprehensive clinical data from the Phase 3, randomized, double-blind, placebo-controlled, multicenter REGAIN study (ECU-MG-301).

Soliris is also approved in the EU for the treatment of refractory gMG in adults who are anti-AChR antibody-positive, and in the U.S. for the treatment of adult patients with gMG who are anti-AChR antibody-positive.

### **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>1,9,10,11</sup> It typically begins with weakness in the muscles that control the movements of the eyeballs 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>11</sup>

In patients with anti-acetylcholine receptor (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>6,7,8</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. As a result, the communication between nerve and muscle is impaired, which in turn leads to a loss of normal muscle function.<sup>1,2</sup>

A subset of patients with anti-AchR antibody-positive gMG fails 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>12,13,14</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.<sup>1,2,3</sup> Complications, exacerbations and myasthenic crises can require hospital and intensive care unit admissions with prolonged stays and can be life-threatening.<sup>4,5</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>12,15,16,17</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 that, 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) and anti-acetylcholine receptor (AChR) antibody-positive myasthenia gravis (MG). Soliris is approved in the U.S., EU, Japan and other countries as the first and only treatment for patients with PNH and aHUS, in the EU as the first and only treatment of refractory generalized MG (gMG) in adults who are anti-AchR antibody-positive, in the U.S. for the treatment of adult patients with gMG who are anti-AchR antibody-positive, and in Japan for the treatment of patients with gMG who are anti-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) 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, and for the treatment of patients with refractory gMG in 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](http://www.soliris.net).

## Important Soliris Safety Information

The U.S. prescribing information for Soliris includes the following warnings and precautions: 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 Centers for Disease Control (CDC)'s Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies. Immunize patients with meningococcal vaccines 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. 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) or at [www.solirisrems.com](http://www.solirisrems.com).

Patients may have increased susceptibility to infections, especially with encapsulated bacteria. Aspergillus infections have occurred in immunocompromised and neutropenic patients. Children treated with Soliris may be at increased risk of developing serious infections due to *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). 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. Administration of Soliris may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions.

In patients with PNH, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, nasopharyngitis, back pain and nausea. In patients with aHUS, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, diarrhea, hypertension, upper respiratory infection,

abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, and pyrexia. In patients with gMG who are anti-AchR antibody-positive, the most frequently reported adverse reaction observed with Soliris treatment in the placebo-controlled clinical study ( $\geq 10\%$ ) was musculoskeletal pain.

## About Alexion

Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases through the innovation, development and commercialization of life-changing therapies. Alexion is the global leader in complement inhibition and has developed and commercializes the first and only approved complement inhibitor to treat patients with paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and anti-acetylcholine receptor (AChR) antibody-positive generalized myasthenia gravis (gMG). In addition, Alexion 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). As the leader in complement biology for over 20 years, 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. 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 Statement

This news release contains forward-looking statements, including statements related to the potential medical benefits of Soliris® (eculizumab) for the treatment of generalized myasthenia gravis (gMG), 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, the risks and uncertainties of drug development, decisions of regulatory authorities regarding the adequacy of our research, 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, failure to satisfactorily address matters raised by the FDA and other regulatory agencies, the possibility that the current rates of adoption of Soliris in paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), or other diseases are not sustained, the possibility that results of clinical trials are not predictive of safety and efficacy results of our products in broader patient populations, 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 at acceptable rates or at all, the outcome of challenges and opposition proceedings to our intellectual property, assertion or potential assertion by third parties that the manufacture, use or sale of our products infringes their intellectual property, 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 (DOJ), the risk that anticipated regulatory filings are delayed, the risk that estimates regarding the number of patients with PNH, aHUS, gMG, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D) are inaccurate, the risks of changing foreign exchange rates, risks relating to the potential effects of the Company's restructuring and relocation of its corporate headquarters, 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 September 30, 2017 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.

## References

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