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New Data from Phase 3 REGAIN Study of Eculizumab (Soliris®) in Patients with Refractory Generalized Myasthenia Gravis (gMG) Presented at ICNMD Annual Congress

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) announced today that researchers presented new results from the REGAIN study, a global, placebo-controlled Phase 3 registration trial of eculizumab (Soliris®) in patients with refractory generalized myasthenia gravis (gMG), at the Hot Topics session of the 14th International Congress on Neuromuscular Diseases (ICNMD) in Toronto. As previously reported, the study's 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. Results presented at ICNMD showed that 18 of 22 pre-defined endpoints and pre-specified analyses in the study, based on the primary and five secondary endpoints, achieved p-values < 0.05.

New secondary efficacy endpoint data presented included change from baseline in Myasthenia Gravis Composite (MGC) score at week 26, which achieved a p-value of 0.1026, and change from baseline in the 15-item Myasthenia Gravis Quality Of Life (MG-QOL15) at week 26, which achieved a p-value of 0.0281, both measured by a worst-rank analysis. A pre-specified sensitivity analysis of the MGC and MG-QOL15 endpoints using repeated measures from baseline to week 26 achieved p-values of 0.0134 and 0.0010, respectively.[1] The full presentation can be found on the Investor page of the Alexion website.

"Although the REGAIN study narrowly missed its primary endpoint, the additional data presented today suggest a magnitude of effect of eculizumab in refractory MG patients across four separate scales of disease severity that is unprecedented in my clinical investigation experience," 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. "These findings are particularly meaningful given the urgent need for a first-ever therapy with the potential to have a transformative impact on patients with refractory MG, who continue to face disabling limitations in their daily lives, including difficulty walking, talking, swallowing, and breathing normally."

P-values Less Than 0.05 Achieved in 18 of 22 Pre-specified Analyses

Outcome Measure	Primary / Secondary Endpoints		Sensitivity Analyses		
	Worst-Rank ANCOVA	Responder Analysis	Repeated Measures at Week 26 (IST as a Covariate)	Change from Baseline at Week 26 or LOCF ANCOVA	Worst-Rank ANCOVA Sensitivity
MG-ADL	0.0698	0.0229	0.0058 (0.0077)	0.0390	0.0800
QMG	0.0129	0.0018	0.0006 (0.0007)	0.0032	0.0169
MGC	0.1026	N/A*	0.0134 (0.0168)	0.0406	0.1084
MG-QOL15	0.0281	N/A*	0.0010 (0.0009)	0.0152	0.0328

*N/A: Not applicable; not a pre-specified analysis

"The MG Community has been waiting for the full results from the REGAIN trial with great interest," said Nancy Law, CEO of the Myasthenia Gravis Foundation of America (MGFA). "There are currently no FDA-approved disease modifying therapies for MG, which means that doctors and patients must often resort to trial and error with medications approved for other conditions to try to manage symptoms. For all too many with MG, the currently available treatment approaches are inadequate in efficacy, or have intolerable side effects. People with MG need more and better treatment options, especially for those with refractory generalized MG, whose extreme muscle weakness can be devastating and even life-threatening. We look forward to advocating for and supporting patients with refractory MG who have a tremendous unmet need."

Detailed Study Results[1]

At ICNMD, Dr. Howard reported that 18 of the study's 22 pre-specified analyses achieved p-values < 0.05. As previously

reported, these included the first three secondary efficacy endpoints of change from baseline to week 26 in Quantitative Myasthenia Gravis (QMG) total score, a physician-administered assessment of MG clinical severity (p=0.0129), as measured by a worst-rank analysis; 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 (p=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 (p=0.0018). The primary efficacy endpoint of change from baseline in MG-ADL total score at week 26 did not reach statistical significance (p=0.0698) as measured by a worst-rank analysis.

Several prospectively defined sensitivity analyses were conducted to validate results for the primary and secondary endpoints, including sensitivity analyses for change from baseline in MG-ADL, QMG, MGC, and MG-QOL15 using repeated measures, all of which achieved p-values < 0.05. As previously reported, the pre-specified sensitivity analyses of the primary and first secondary endpoints of MG-ADL and QMG using repeated measures had p-values of 0.0058 and 0.0006, respectively. The pre-specified sensitivity analyses of MGC and MG-QOL15 using repeated measures at week 26 showed a mean change from baseline in MGC with eculizumab treatment at week 26 of -8.1 versus a mean change with placebo of -4.8 (p=0.0134), and a mean change from baseline in MG-QOL15 with eculizumab treatment at week 26 of -12.6 versus a mean change with placebo of -5.4 (p=0.0010).

Additional results from the study, including detailed outcomes from the MG-ADL and QMG responder analyses, were presented at ICNMD.

"While the REGAIN study narrowly missed statistical significance on the primary endpoint, the totality of data from this landmark trial supports the potential of eculizumab to provide an early, sustained, and substantial response in patients with refractory gMG. Notably, 18 out of 22 pre-specified endpoints and analyses achieved p-values less than 0.05 for patients treated with eculizumab compared to placebo, underscoring the pivotal role of complement inhibition in addressing the underlying cause of disease," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "Today, there are no effective treatments for the ultra-rare segment of patients with gMG who are refractory to conventional therapies and continue to suffer from profound, complement-mediated muscle weakness. Alexion is committed to addressing the urgent needs of this patient population, and we look forward to discussing study results with U.S. and EU regulators."

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%), nausea (12.9%, 14.3%), and myasthenia gravis (9.7%, 17.5%). 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. Half as many patients treated with eculizumab received rescue therapy compared with placebo (9.7%, 19.0%).

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 ≥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, as well as the three secondary endpoints that involved changes from baseline—QMG, MGC, and MG-QOL15—were assessed using a worst-rank analysis.

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.[2,3,4]

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.[5] 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.[6,7,8] Patients with refractory gMG frequently require hospitalization, often involving intensive care unit stays.[9]

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 on Soliris, including the full U.S. prescribing information, is available at 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 [see Warnings and Precautions (5.1)]. 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 Warnings and Precautions (5.1) for additional guidance on the management of the risk 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 [see Warnings and Precautions (5.2)]. 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 headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, and pyrexia. Soliris is not indicated for the treatment of patients with Shiga-toxin *E. coli*-related hemolytic uremic syndrome (STEC-HUS). Please see full prescribing information for Soliris, including BOXED WARNING regarding risk of serious meningococcal infection.

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 commercializes 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.

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Forward-Looking Statements

This news release contains forward-looking statements, including statements related to the potential medical benefits of eculizumab (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.

References

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