Alexion Announces Positive Topline Results from Phase 3 Study of ULTOMIRIS® (ravulizumab-cwvz) in Adults with Generalized Myasthenia Gravis (gMG)

July 15, 2021

– Study met primary endpoint of change from baseline in the Myasthenia Gravis-Activities of Daily Living Profile (MG-ADL) total score at Week 26 –

– ULTOMIRIS demonstrated compelling efficacy as early as Week 1, sustained for 52 weeks –

BOSTON--(BUSINESS WIRE)--Jul. 15, 2021-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced positive topline results from a Phase 3 study evaluating the safety and efficacy of ULTOMIRIS® (ravulizumab-cwvz) in adults with generalized myasthenia gravis (gMG). The study met, with high statistical significance, its primary endpoint of change from baseline in the Myasthenia Gravis-Activities of Daily Living Profile (MG-ADL) total score, a patient-reported assessment, at Week 26, and for the subset of patients who have completed 26 weeks in the extension study to date, the positive treatment effect was maintained through a total of 52 weeks. ULTOMIRIS was well tolerated with a safety profile consistent with that observed in Phase 3 studies in paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS). Based on these results, Alexion plans to make regulatory filings in the U.S., European Union and Japan in late 2021/early 2022.

“The treatment landscape for people living with gMG has advanced and expanded rapidly in recent years, empowering both patients and caregivers. However, as a clinician and scientist, I know the work is not done,” said Professor James F. Howard, M.D., Department of Neurology at The University of North Carolina, Chapel Hill, USA, and lead primary investigator in the Phase 3 study. “These Phase 3 ULTOMIRIS results reinforce the critical role complement inhibition plays in treating gMG. I am encouraged by the opportunity this could provide for more patients to be treated early with a mechanism of action designed to preserve neuromuscular function.”

“The approval of SOLIRIS was a critically important first step in addressing the urgent need for a treatment for people with severe symptoms and complications of MG, and was the first new treatment for this devastating disease in more than 60 years. Today’s results demonstrate that ULTOMIRIS may help a broader range of patients than was studied in the SOLIRIS Phase 3 trial, including those with milder symptoms or earlier in their treatment journey, while still offering clinically meaningful benefits that were seen as early as Week 1 and maintained up to 52 weeks,” said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. “These data provide confidence that ULTOMIRIS has the potential to become the new standard of care for gMG and may reduce patient burden with its less frequent dosing schedule, leading to better treatment adherence and patient satisfaction. We are working to prepare regulatory submissions in the U.S., EU and Japan as quickly as possible.”

About the Phase 3 Study
This global Phase 3 randomized, double-blind, placebo-controlled, multicenter 26-week study evaluated the safety and efficacy of ULTOMIRIS in adults with gMG who were not previously treated with a complement inhibitor medicine. The study enrolled 175 patients across North America, Europe, Asia-Pacific and Japan. To enter the study, participants were required to have a confirmed MG diagnosis at least 6 months prior to the screening visit with a positive serologic test for anti-AChR antibodies, MG-ADL total score of at least 6 at study entry and Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV at screening. There was no requirement for prior treatment failure, and patients could stay on stable standard of care medicines, with a few exceptions, for the duration of the study.

Patients were randomized 1:1 to receive ULTOMIRIS or placebo for a total of 26 weeks. Patients received a single weight-based loading dose on Day 1, followed by regular weight-based maintenance dosing beginning on Day 15, every 8 weeks. The primary endpoint of change from baseline in the Myasthenia Gravis-Activities of Daily Living Profile (MG-ADL) total score at Week 26 was assessed along with multiple secondary endpoints evaluating improvement in disease-related and quality of life measures.

The study met its primary endpoint, with a statistically significant change in MG-ADL score from baseline through Week 26 for patients receiving ULTOMIRIS compared to those receiving placebo (ULTOMIRIS: -3.1, placebo: -1.4, treatment difference: -1.6, $p<0.001$).

In the prospectively-defined secondary endpoints of change from baseline through Week 26 in Quantitative Myasthenia Gravis (QMG) total score – a physician-administered assessment of MG clinical severity – as well as the proportion of patients who achieved an improvement of at least 5 points in QMG, ULTOMIRIS also demonstrated clinically meaningful and statistically significant improvements ($p<0.001$ and $p=0.005$, respectively). Nearly three times as many patients receiving ULTOMIRIS experienced an improvement of at least 5 points in their QMG score compared to patients receiving placebo (30.0% vs 11.3%). These improvements in MG-ADL and QMG scores were observed as early as Week 1 and were sustained through Week 26.

Additional secondary endpoints assessing qualify of life measures, such as Revised 15-Component Myasthenia Gravis Quality of Life (MG-QOL15r) score ($p=0.064$) and Neuro-QOL Fatigue score ($p=0.373$), did not meet statistical significance at Week 26. The proportion of patients who achieved an improvement of at least 3 points in MG-ADL score (ULTOMIRIS: 56.7%, placebo: 34.1%, nominal $p=0.005$), was not considered statistically significant based on hierarchical testing.

During the randomized controlled period, adverse events were comparable between the ULTOMIRIS and placebo groups. The most frequently observed adverse events were headache (ULTOMIRIS: 18.6%; placebo: 25.8%), diarrhea (ULTOMIRIS: 15.1%; placebo: 12.4%) and nausea (ULTOMIRIS: 10.5%; placebo: 10.1%). The most frequently observed serious adverse events were MG crisis (ULTOMIRIS: 1.2%) and MG worsening (placebo: 3.4%).

Through 52 weeks (26 weeks randomized controlled period + 26 weeks of open-label extension), there were four patient deaths in the ULTOMIRIS group – three of them were due to COVID-19 and none were considered related to treatment with ULTOMIRIS. No cases of meningococcal infection were observed through 52 weeks.

Patients who completed the randomized controlled period were eligible to continue into an open-label extension period evaluating the safety and efficacy of ULTOMIRIS for up to two years, which is ongoing. At the time of this preliminary analysis of the open-label extension period, 75 patients had completed 26 weeks of treatment, for a total of 52 weeks of treatment. Among the patients who received ULTOMIRIS in the randomized controlled period, the treatment effects were maintained through an additional 26 weeks of treatment, demonstrating sustained efficacy for a total of 52 weeks. In addition, patients who received placebo in the randomized controlled period and switched to ULTOMIRIS at the beginning of the open-label extension showed immediate and sustained improvement in MG-ADL and QMG scores in a similar magnitude and time course to that observed in the ULTOMIRIS group during the randomized controlled period.

About Generalized Myasthenia Gravis
Generalized myasthenia gravis (gMG) is a rare autoimmune disorder characterized by severe muscle weakness. In gMG, inflammation causes damage at the connection point between nerve cells and the muscles they control (known as the neuromuscular junction or NMJ). This damage leads to a breakdown of communication between the brain and muscles, causing loss of muscle function and severe weakness.

About 85 percent of people with gMG produce specific antibodies that bind to the surface of the cells at the NMJ. This binding activates the complement cascade and causes the immune system to attack the NMJ. People with gMG can suffer from initial symptoms, such as slurred speech, droopy eyelids, double vision, and lack of balance, which can often lead to more severe symptoms like choking, impaired swallowing, extreme fatigue and even episodes of respiratory failure.

gMG can occur at any age, but it most commonly begins for women before the age of 40 and for men after the age of 60. The prevalence of gMG is estimated at 107 to 278 per million people.

About ULTOMIRIS®
ULTOMIRIS® (ravulizumab) is the first and only long-acting C5 complement inhibitor. The medication works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system. When activated in an uncontrolled manner, the complement cascade over-responds, leading the body to attack its own healthy cells. ULTOMIRIS is administered intravenously every eight weeks or, for pediatric patients less than 20 kg, every four weeks, following a loading dose. ULTOMIRIS is approved in the United States for the treatment of adults and children (one month of age and older) with paroxysmal nocturnal hemoglobinuria (PNH), as well as in the European Union (EU) and Japan as a treatment for adults with PNH. It is also approved in the U.S. and Japan for atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA) in adult and pediatric (one month of age and older) patients, as well as in the EU for the treatment of adults and children with a body weight of at least 10 kg with aHUS. To learn more about the regulatory status of ULTOMIRIS in the countries that we serve, please visit www.alexion.com.

INDICATIONS & IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz)

INDICATIONS
What is ULTOMIRIS?
ULTOMIRIS is a prescription medicine used to treat:

- adults and children 1 month of age and older with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH).
- adults and children 1 month of age and older with a disease called atypical Hemolytic Uremic Syndrome (aHUS). ULTOMIRIS is not used in treating people with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

It is not known if ULTOMIRIS is safe and effective in children younger than 1 month of age.

IMPORTANT SAFETY INFORMATION
What is the most important information I should know about ULTOMIRIS?
ULTOMIRIS is a medicine that affects your immune system and can lower the ability of your immune system to fight infections.

- ULTOMIRIS increases your chance of getting serious and life-threatening meningococcal infections that may quickly become life-threatening and cause death if not recognized and treated early.

1. You must receive meningococcal vaccines at least 2 weeks before your first dose of ULTOMIRIS if you are not vaccinated.
2. If your doctor decided that urgent treatment with ULTOMIRIS is needed, you should receive meningococcal vaccination as soon as possible.
3. If you have not been vaccinated and ULTOMIRIS therapy must be initiated immediately, you should also receive 2 weeks of antibiotics with your vaccinations.
4. If you had a meningococcal vaccine in the past, you might need additional vaccination. Your doctor will decide if you need additional vaccination.
5. Meningococcal vaccines reduce but do not prevent all meningococcal infections. Call your doctor or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection: 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.

Your doctor will give you a Patient Safety Card about the risk of meningococcal infection. Carry it with you at all times during treatment and for 8 months after your last ULTOMIRIS dose. It is important to show this card to any doctor or nurse to help them diagnose and treat you quickly.

ULTOMIRIS is only available through a program called the ULTOMIRIS REMS. Before you can receive ULTOMIRIS, your doctor must: enroll in the ULTOMIRIS REMS program; counsel you about the risk of meningococcal infection; give you information and a **Patient Safety Card** about the symptoms and your risk of meningococcal infection (as discussed above); and make sure that you are vaccinated with a meningococcal vaccine, and if needed, get revaccinated with the meningococcal vaccine. Ask your doctor if you are not sure if you need to be revaccinated.

ULTOMIRIS may also increase the risk of other types of serious infections. Make sure your child receives vaccinations against *Streptococcus*

pneumoniae and *Haemophilis influenzae* type b (Hib) if treated with ULTOMIRIS. Call your doctor right away if you have any new signs or symptoms of infection.

Who should not receive ULTOMIRIS?
Do not receive ULTOMIRIS if you have a meningococcal infection or have not been vaccinated against meningococcal infection unless your doctor decides that urgent treatment with ULTOMIRIS is needed.

Before you receive ULTOMIRIS, tell your doctor about all of your medical conditions, including if you: have an infection or fever, are pregnant or plan to become pregnant, and are breastfeeding or plan to breastfeed. It is not known if ULTOMIRIS will harm your unborn baby or if it passes into your breast milk. You should not breastfeed during treatment and for 8 months after your final dose of ULTOMIRIS.

Tell your doctor about all the vaccines you receive and medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements which could affect your treatment.

If you have PNH and you stop receiving ULTOMIRIS, your doctor will need to monitor you closely for at least 16 weeks after you stop ULTOMIRIS. Stopping ULTOMIRIS may cause breakdown of your red blood cells due to PNH. Symptoms or problems that can happen due to red blood cell breakdown include: drop in your red blood cell count**,** tiredness**,** blood in your urine**,** stomach-area (abdomen) pain**,** shortness of breath**,** blood clots**,** trouble swallowing, and erectile dysfunction (ED) in males.

If you have aHUS, your doctor will need to monitor you closely for at least 12 months after stopping treatment for signs of worsening aHUS or problems related to a type of abnormal clotting and breakdown of your red blood cells called thrombotic microangiopathy (TMA). Symptoms or problems that can happen with TMA may include: confusion or loss of consciousness, seizures, chest pain (angina), difficulty breathing and blood clots or stroke.

What are the possible side effects of ULTOMIRIS?

ULTOMIRIS can cause serious side effects including infusion-related reactions. Symptoms of an infusion-related reaction with ULTOMIRIS may include lower back pain, feeling faint or discomfort in your arms or legs. Tell your doctor or nurse right away if you develop these symptoms, or any other symptoms during your ULTOMIRIS infusion that may mean you are having a serious infusion reaction, including: chest pain, trouble breathing or shortness of breath, swelling of your face, tongue, or throat, and feel faint or pass out.

The most common side effects of ULTOMIRIS in people treated for PNH are upper respiratory tract infection and headache.

The most common side effects of ULTOMIRIS in people with aHUS are upper respiratory tract infection, diarrhea, nausea, vomiting, headache, high blood pressure and fever.

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects of ULTOMIRIS. For more information, ask your doctor or pharmacist. Call your doctor right away if you miss an ULTOMIRIS infusion or for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see the accompanying full Prescribing Information and Medication Guide for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections/sepsis.

About Alexion
Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialization of life-changing medicines. As a leader in rare diseases for more than 25 years, Alexion has developed and commercializes two approved complement inhibitors to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), as well as the first and only approved complement inhibitor to treat anti-acetylcholine receptor (AchR) antibody-positive generalized myasthenia gravis (gMG) and 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) as well as the first and only approved Factor Xa inhibitor reversal agent. In addition, the company is developing several mid-to-late-stage therapies, including a copper-binding agent for Wilson disease, an anti-neonatal Fc receptor (FcRn) antibody for rare Immunoglobulin G (IgG)-mediated diseases and an oral Factor D inhibitor as well as several early-stage therapies, including one for light chain (AL) amyloidosis, a second oral Factor D inhibitor and a third complement inhibitor. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on hematology, nephrology, neurology, metabolic disorders, cardiology, ophthalmology and acute care. Headquartered in Boston, Massachusetts, Alexion 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

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Forward-Looking Statements
This press release contains forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Alexion and its products, including statements related to: the anticipated benefits of ULTOMIRIS for gMG patients; Alexion plans to make regulatory filings in the U.S., European Union and Japan in late 2021/early 2022; ULTOMIRIS has the opportunity to provide more patients that are treated early with a mechanism of action designed to preserve neuromuscular function; ULTOMIRIS may help a broader range of patients than was studied in the SOLIRIS Phase 3 trial; ULTOMIRIS has the potential to become the new standard of care for gMG and may reduce patient burden with its less frequent dosing schedule, leading to better treatment adherence and patient satisfaction; and ULTOMIRIS' continued safety and efficacy profile.

Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ materially from those expected by these forward looking statements, including for example: ULTOMIRIS may not be approved for use by regulatory agencies (or such approval may be delayed); the filing of requests for regulatory approval may not ultimately be submitted (or may be delayed); ULTOMIRIS may not generate the expected benefits to patients (or the healthcare system) that are anticipated; anticipated regulatory approvals may be delayed or refused; the Company may experience delays (or be prevented) for obtaining approval or commencing or continuing sales of ULTOMIRIS for gMG, due to manufacturing or other reasons; results of clinical trials may not be sufficient to satisfy regulatory authorities to approve ULTOMIRIS as a treatment for gMG and/or other indication (or they may request additional trials or additional information); results in clinical trials may not be indicative of results from later stage or larger clinical

trials (or the use in broader patient populations once the product is approved for use by regulatory agencies); the possibility that results of clinical trials are not predictive of safety and efficacy and potency of our products including ULTOMIRIS (or we fail to adequately operate or manage our clinical trials) which could cause us to discontinue sales of the product (or halt trials, delay or prevent us from making regulatory approval filings or result in denial of approval of our product candidates); the severity of the impact of the COVID-19 pandemic on Alexion's business, including on commercial and clinical trial and clinical development programs; unexpected delays in clinical trials; unexpected concerns regarding products and product candidates that may arise from additional data or analysis obtained during clinical trials or obtained once used by patients following product approval; future product improvements may not be realized due to expense or feasibility or other factors; delays (expected or unexpected) in the time it takes regulatory agencies to review and make determinations on applications for the marketing approval of our products; inability to timely submit (or failure to submit) future applications for regulatory approval for our products and product candidates; inability to timely initiate (or failure to initiate) and complete future clinical trials due to safety issues, IRB decisions, CMC-related issues, expense or unfavorable results from earlier trials (among other reasons); our dependence on sales from our complement inhibitors; future competition from biosimilars and novel products; decisions of regulatory authorities regarding the adequacy of our research, marketing approval or material limitations on the marketing of our products; delays or the inability to launch product candidates due to regulatory restrictions, anticipated expense, manufacturing issues, or other matters; interruptions or failures in the manufacture and supply of our products and our product candidates; failure to satisfactorily address matters raised by regulatory agencies regarding products and product candidates; uncertainty of long-term success in developing, licensing or acquiring other product candidates or additional indications for existing products; the possibility that current rates of adoption of our products are not sustained; the adequacy of our pharmacovigilance and drug safety reporting processes; failure to protect and enforce our data, intellectual property and proprietary rights and the risks and uncertainties relating to intellectual property claims, lawsuits and challenges against us (including intellectual property lawsuits relating to ULTOMIRIS brought by third parties); 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; failure to realize the benefits and potential of investments, collaborations, licenses and acquisitions; the possibility that expected tax benefits will not be realized; potential declines in sovereign credit ratings or sovereign defaults in countries where we sell our products; delay of collection or reduction in reimbursement due to adverse economic conditions or changes in government and private insurer regulations and approaches to reimbursement; adverse impacts on our supply chain, clinical trials, manufacturing operations, financial results, liquidity, hospitals, pharmacies and health care systems from natural disasters and global pandemics, including the coronavirus; uncertainties surrounding legal proceedings, company investigations and government investigations; the risk that estimates regarding the number of patients with PNH, aHUS, gMG, NMOSD, HPP and LAL-D and other indications we are pursuing are inaccurate; the impact of the proposed transaction between Alexion and AstraZeneca plc; the risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructurings; 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 quarter ended March 31, 2021 and in our other filings with the SEC. Alexion disclaims any obligation 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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