Alexion Announces Planned Initiation of Pivotal Phase 3 Study of ULTOMIRIS® (ravulizumab) in ALS

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- 50-week global study to enroll ~350 patients across broad ALS population -

BOSTON--(BUSINESS WIRE)--Jan. 14, 2020-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced the planned initiation of a pivotal Phase 3 study of ULTOMIRIS® (ravulizumab) in amyotrophic lateral sclerosis (ALS). The 50-week global study, called CHAMPION-ALS, will evaluate approximately 350 adults across a broad patient population, and the primary endpoint will be change in ALS functional rating scale-revised (ALSFRS-R) score. Alexion submitted an investigational new drug application (IND) for ULTOMIRIS in ALS to the FDA in the fourth quarter of 2019 and plans to initiate the Phase 3 study this quarter.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20200114005254/en/

“Given the significant need for new and improved treatments for ALS, we are committed to advancing this clinical program with urgency,” said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. “Based on preclinical data and the significant role complement activation is known to play in other neuromuscular diseases, we believe ULTOMIRIS has the potential to inhibit complement-mediated damage in people with ALS, which may slow disease progression. We thank the ALS community for their involvement in designing this Phase 3 program and look forward to continued close collaboration as we move it forward.”

“We’ve made great progress advancing ALS research in recent years, but there is still more work to be done to ensure patients benefit from these advances in the form of new treatments,” said Calaneet Balas, CEO and President of The ALS Association. “It’s great that Alexion, which has an established record of bringing new treatments to patients with devastating rare diseases, is joining the fight against ALS.”

About the Phase 3 CHAMPION-ALS Study
The Phase 3 CHAMPION-ALS trial is a randomized, double-blind, placebo-controlled multicenter global study designed to evaluate the efficacy and safety of ULTOMIRIS across a broad ALS population. The study will enroll approximately 350 adults with sporadic or familial ALS who have had disease onset (in the form of first motor symptoms) within the prior 36 months, demonstrate a slow vital capacity (SVC) of at least 65 percent predicted, and are not dependent on respiratory support.

Study participants will be randomized on a 2:1 basis to receive ULTOMIRIS or placebo every 8 weeks following an initial loading dose and may continue to receive their existing standard of care treatment for ALS. After 50 weeks, all patients will receive ULTOMIRIS in a 2-year open-label extension phase of the study. The study will be conducted at approximately 90 clinical trial sites across North America, Europe and Asia-Pacific.

The primary study endpoint will be change from baseline in ALS functional rating scale-revised (ALSFRS-R) score. Secondary endpoints will include ventilation assistance-free survival (VAFS), respiratory capacity, muscle strength, neurofilament light chain (NfL) serum concentrations and safety.

About ALS
Amyotrophic lateral sclerosis (ALS) is a neurological disorder characterized by progressive degeneration of nerve cells (motor neurons) in the brain and the spinal cord that control muscles throughout the body. When the nerve cells die, the brain can no longer initiate and control muscle movement, which results in severe disability, paralysis and eventually death.

ALS is a relentlessly progressive disorder. People with ALS may lose the ability to speak, eat, move and breathe. The rate of progression between individuals is variable and the natural history generally reflects progressive worsening over time until death occurs. The average life expectancy from symptom onset is between two and five years. Currently approved medications may slow disease progression, but ALS management is mostly supportive, palliative and symptom based.

An estimated 15,000 to 20,000 people are living with ALS across the United States, France, Germany, Italy, Spain, the United Kingdom and Japan. There are two different types of ALS, sporadic and familial. Sporadic, which is the most common form of the disease, accounts for 85 to 90 percent of cases and may affect anyone, anywhere. Familial ALS, the inherited form of the disease, accounts for 10 to 15 percent of cases.

About ULTOMIRIS® (ravulizumab-cwvz)
ULTOMIRIS® (ravulizumab-cwvz) is the first and only approved long-acting C5 complement inhibitor. It is administered intravenously every eight weeks or every four weeks for pediatric patients less than 20 kg, following a loading dose. ULTOMIRIS works by inhibiting the C5 protein in the terminal complement cascade, a part of the body’s immune system. The terminal complement cascade, when activated in an uncontrolled manner, plays a role in severe ultra-rare disorders. ULTOMIRIS is approved in the U.S., Japan, and the EU as a treatment for adults with PNH and in the U.S. for aHUS to inhibit complement-mediated thrombotic microangiopathy (TMA) in adult and pediatric (one month of age and older) patients.

INDICATIONS & IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS (ravulizumab-cwvz) 300 mg / 30 mL injection for intravenous use
INDICATIONS
ULTOMIRIS is a prescription medicine called a monoclonal antibody. ULTOMIRIS is used to treat adults with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH). ULTOMIRIS is used to treat 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 with PNH. It is not known if ULTOMIRIS is safe and effective in children younger than 1 month of age in aHUS.

IMPORTANT SAFETY INFORMATION
ULTOMIRIS is a medicine that affects the immune system. ULTOMIRIS can lower the ability of the immune system to fight infections. ULTOMIRIS

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

Meningococcal vaccines must be received at least 2 weeks before the first dose of ULTOMIRIS if one has not already had this vaccine. If one's doctor decides that urgent treatment with ULTOMIRIS is needed, meningococcal vaccination should be administered as soon as possible. If one has not been vaccinated and ULTOMIRIS therapy must be initiated immediately, 2 weeks of antibiotics should also be administered with the vaccinations. If one had a meningococcal vaccine in the past, additional vaccination might be needed before starting ULTOMIRIS. One's doctor will decide if additional meningococcal vaccination is needed. Meningococcal vaccines reduce the risk of meningococcal infection but do not prevent all meningococcal infections. Call one's doctor or get emergency medical care right away if any of these signs and symptoms of a meningococcal infection occur: 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. One's doctor will give a Patient Safety Card about the risk of meningococcal infection. Carry the card at all times during treatment and for 8 months after your the ULTOMIRIS dose.

ULTOMIRIS is only available through a program called the **ULTOMIRIS REMS**.

ULTOMIRIS may also increase the risk of other types of serious infections. People who take ULTOMIRIS may have an increased risk of getting infections caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*. Certain people may also have an increased risk of gonorrhea infection. To find out if one is at risk for gonorrhea infection, about gonorrhea prevention, and regular testing, talk to the doctor. Call the doctor right away if one has any new signs or symptoms of infection.

Do not receive ULTOMIRIS if one has a meningococcal infection, or has not been vaccinated against meningococcal infection unless the doctor decides that urgent treatment with ULTOMIRIS is needed.

Before one receives ULTOMIRIS, tell the doctor about all of the medical conditions, including if one: has 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 an unborn baby. It is not known if ULTOMIRIS passes into the breast milk. One should not breastfeed during treatment and for 8 months after one's final dose of ULTOMIRIS.

Tell the doctor about all the medicines one takes, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ULTOMIRIS and other medicines can affect each other causing side effects. Know the medicines one takes and the vaccines one receives. Keep a list of them to show the doctor and pharmacist when one gets a new medicine.

If one has PNH and stops receiving ULTOMIRIS, the doctor will need to monitor closely for at least 16 weeks after one stops ULTOMIRIS. Stopping ULTOMIRIS may cause breakdown of the red blood cells due to PNH. Symptoms or problems that can happen due to red blood cell breakdown include: drop in the red blood cell count, tiredness, blood in the urine, stomach-area (abdomen) pain, shortness of breath, blood clots, trouble swallowing, and erectile dysfunction (ED) in males. If one has aHUS, the doctor will need to monitor closely for at least 12 months after stopping treatment for signs of worsening aHUS symptoms or problems related to a type of abnormal clotting and breakdown of the 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. If one misses an ULTOMIRIS infusion, call the doctor right away.

ULTOMIRIS can cause serious side effects including infusion reactions. Infusion reactions may happen during one's ULTOMIRIS infusion. Symptoms of an infusion reaction with ULTOMIRIS may include lower back pain, pain with the infusion, feeling faint or discomfort in the arms or legs. Tell the doctor or nurse right away if these symptoms develop, or any other symptoms during the ULTOMIRIS infusion that may mean one is having a serious infusion reaction, including: chest pain, trouble breathing or shortness of breath, swelling of the face, tongue, or throat, and feel faint or pass out. One's doctor will treat the symptoms as needed.

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

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 through the discovery, development and commercialization of life-changing therapies. As the global leader in complement biology and inhibition for more than 20 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). In addition, the company is developing several mid-to-late-stage therapies, including a second complement inhibitor, a copper-binding agent for Wilson disease and an anti-neonatal Fc receptor (FcRn) antibody for rare Immunoglobulin G (IgG)-mediated diseases as well as several early-stage therapies, including one for light chain (AL) amyloidosis and a second anti-FcRn therapy. 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, metabolic disorders and cardiology. 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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For patient or advocacy inquiries please contact patientadvocacy@alexion.com.

Forward-Looking Statement
This press release contains forward-looking statements, including statements related to: Alexion's future plans to initiate a pivotal Phase 3 study of ULTOMIRIS® (ravulizumab) in ALS; ULTOMIRIS has the potential to inhibit complement-mediated damage in people with ALS, which may slow disease progression, based on preclinical data and the significant role complement activation is known to play in other neuromuscular diseases; the potential benefits of ULTOMIRIS to people with ALS; anticipated future continued close collaboration with the ALS community as Alexion moves forward with the clinical trial; the protocol and method of the ULTOMIRIS clinical trial; and the timing of anticipated completion of clinical trials.

Forward-looking statements involve risks and uncertainties relating to future events and the future performance of Alexion and 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: drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product; the initiation of a pivotal Phase 3 study of ULTOMIRIS in ALS may be delayed or may never be initiated; the results of the pivotal Phase 3 study of ULTOMIRIS in ALS may not result in regulatory approval necessary to commercialize ULTOMIRIS for this indication (or regulatory authorities may require additional trials to confirm safety and efficacy of ULTOMIRIS in ALS prior to approval which would be expensive and time-consuming); ULTOMIRIS may not gain market acceptance and/or may not be recognized by patients and physicians as a treatment for ALS; the benefits (including safety and efficacy), if any, of ULTOMIRIS evidenced in clinical trials may not be witnessed in a broader patient population; any potential post-approval restrictions that regulatory authorities may impose on ULTOMIRIS as a treatment for ALS; future competition from biosimilars and other 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 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 with respect to product candidates; results in early stage clinical trials may not be indicative of full results or results from later stage or larger clinical trials (or broader patient populations) and do not ensure regulatory approval; the possibility that results of clinical trials are not predictive of safety and efficacy and potency of our products (or we may fail to adequately operate or manage our clinical trials) which could cause us to halt trials, delay or prevent us from making regulatory approval filings or result in denial of approval of our product candidates; unexpected delays in clinical trials; 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 and challenges against us (including intellectual property lawsuits relating to ULTOMIRIS brought by third parties against Alexion); 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; uncertainties surrounding legal proceedings (including intellectual property suits initiated against Alexion and our products), company investigations and government investigations, including investigations of Alexion by the U.S. Securities and Exchange Commission (SEC) and U.S. Department of Justice; the risks of changing foreign exchange rates; 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, 2019 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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Source: Alexion Pharmaceuticals, Inc.

Media
Megan Goulart, 857-338-8634
Senior Director, Corporate Communications

Investors
Susan Altschuller, Ph.D., 857-338-8788
Vice President, Investor Relations