Alexion Announces FDA Approval of ULTOMIRIS® (ravulizumab-cwvz) for Children and Adolescents with Paroxysmal Nocturnal Hemoglobinuria (PNH)

June 7, 2021

– With this approval, ULTOMIRIS is the first and only medicine approved in the U.S. to treat children and adolescents with PNH –

– Approval based on interim results from Phase 3 study showing ULTOMIRIS demonstrated complete terminal complement inhibition through 26 weeks –

BOSTON--(BUSINESS WIRE)--Jun. 7, 2021-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced the U.S. Food and Drug Administration (FDA) has approved the expanded use of ULTOMIRIS® (ravulizumab-cwvz) to include children (one month of age and older) and adolescents with paroxysmal nocturnal hemoglobinuria (PNH). ULTOMIRIS, a long-acting C5 inhibitor that offers immediate, complete and sustained complement inhibition, is now the first and only FDA-approved medicine for children and adolescents with PNH.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20210607005638/en/

Image of ULTOMIRIS® (ravulizumab-cwvz) 100 mg/mL vials (3 mL and 11 mL). (Photo: Business Wire)

"It can take months, and sometimes years, to receive a correct diagnosis for PNH — a chronic, progressive and potentially life-threatening rare disease – which can be an overwhelming experience for children and their families," said Satheesh Chonat, M.D., principal investigator for the pediatric clinical trial and pediatric hematologist and oncologist at the Aflac Cancer & Blood Disorders Center at Children's Healthcare of Atlanta, as well as assistant professor of pediatrics at the Emory University School of Medicine. "Managing the disease can be extremely burdensome for these children and their families, who often miss school and work for infusions, blood transfusions, and medical appointments. It's exciting to finally have an approved medicine for these patients who are diagnosed as children."

Since its initial approval in 2018, ULTOMIRIS has quickly become the standard of care in the U.S. for the treatment of adults with PNH. PNH is a complement-mediated disease, which means the symptoms and complications are caused by a lack of regulation, or control, of the complement system, an essential part of the immune system. ULTOMIRIS is designed to target the part of the complement system at the site of disease activity (terminal complement), while preserving function of other parts of the immune system to be able to fight common pathogens and infections. ULTOMIRIS reduces red blood cell destruction in the blood vessels, also known as intravascular hemolysis, and thrombosis (blood clot) risk by providing immediate, complete, and sustained terminal complement inhibition.

"This expanded approval is a significant step forward for the PNH community as we work to elevate awareness of this rare disease in children and adolescents and ensure patients, both pediatric and adult, have meaningful treatment options available," said Janice Frey-Angel, Chief Executive Officer and Executive Director of the Aplastic Anemia and Myelodysplastic Syndrome International Foundation (AAMDSIF). "PNH can have significant physical, emotional and/or psychological impacts on families, and we are pleased there is now an approved medicine for the younger members of our community and the families who care for them."

This approval is based on interim Phase 3 study results, which showed that ULTOMIRIS was effective in achieving complete C5 complement inhibition through 26 weeks in children and adolescents up to 18 years of age. Additionally, ULTOMIRIS had no reported treatment-related severe adverse events, and no patients discontinued treatment during the primary evaluation period or experienced breakthrough hemolysis, which can lead to disabling or potentially fatal blood clots. The efficacy and safety of ULTOMIRIS in children and adolescents is consistent with the established profile of ULTOMIRIS in clinical studies involving adults with PNH and is representative of the broad PNH patient population seen in the real-world clinical

setting. The results of the pediatric study continue to demonstrate Alexion's commitment to treating complement-mediated diseases, which spans more than 17 clinical trials – including the largest pediatric and adult trials in PNH completed to date – and over 60,000 patient-years of trial and real-world data, across more than 50 countries. Data from the interim analysis will be presented as an e-poster during the European Hematology Association 2021 Virtual Congress and will be made available on the congress website on June 11, 2021 at 9:00 a.m. CEST (3:00 a.m. EDT).

"PNH can have a profound impact on a child's development and quality of life. With its established safety and efficacy profile, ULTOMIRIS has the potential to transform the lives of children and adolescents suffering from this devastating rare disease," said John Orloff, M.D., Executive Vice President and Head of Research and Development at Alexion. "We are inspired by the bravery and resilience of the children and adolescents, as well as their families, who participated in the study, and we are grateful for their commitment — as well as that of the trial investigators — to advancing the understanding of PNH and disease management in younger people. We also appreciate the sense of urgency shown by regulators in prioritizing reviewing and approving the first treatment in the U.S. for children and adolescents with PNH."

Alexion plans to make ULTOMIRIS available to pediatric patients in the U.S. immediately. A regulatory filing for ULTOMIRIS in pediatric patients with PNH is under review in the European Union (EU).

About Paroxysmal Nocturnal Hemoglobinuria (PNH)

PNH is a serious ultra-rare blood disorder with devastating consequences. It is characterized by the destruction of red blood cells, which is also referred to as hemolysis. PNH occurs when the complement system—a part of the body's immune system—over-responds, leading the body to attack its own red blood cells. PNH often goes unrecognized, with delays in diagnosis from one to more than five years. Patients with PNH may experience a range of symptoms, such as fatigue, difficulty swallowing, shortness of breath, abdominal pain, erectile dysfunction, dark-colored urine and anemia. The most devastating consequence of chronic hemolysis is the formation of blood clots, which can occur in blood vessels throughout the body, damage vital organs, and potentially lead to premature death. The prognosis of PNH can be poor in many cases, so a timely and accurate diagnosis — in addition to appropriate treatment — is critical to improving patient outcomes

About ULTOMIRIS®

ULTOMIRIS® (ravulizumab-cwvz) 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 (U.S.) 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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For patient or advocacy inquiries please contact *patientadvocacy@alexion.com*.

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 PNH patients (including children and adolescents);

ULTOMIRIS' continued safety and efficacy profile; anticipated timing to receive a correct diagnosis for PNH; ULTOMIRIS' expanded approval is a significant step forward for the PNH community; PNH can have a profound impact on a child's development and quality of life; with its established safety and efficacy profile, ULTOMIRIS has the potential to transform the lives of children and adolescents suffering from this devastating rare disease; and Alexion plans to make ULTOMIRIS available to pediatric patients in the U.S. immediately. 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 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), due to manufacturing or other reasons, from making available ULTOMIRIS to pediatric patients in the U.S. immediately; results of clinical trials may not be sufficient to satisfy regulatory authorities to approve ULTOMIRIS as a treatment for PNH and/or aHUS 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 in broader patient populations (including children and adolescents) 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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