



## Alexion Receives FDA Approval for ULTOMIRIS® (ravulizumab-cwvz) for Atypical Hemolytic Uremic Syndrome (aHUS)

October 18, 2019

- At 26 weeks, 54% of adults and 71% of children treated with ULTOMIRIS demonstrated Complete Thrombotic Microangiopathy (TMA) Response -

BOSTON--(BUSINESS WIRE)--Oct. 18, 2019-- [Alexion Pharmaceuticals, Inc.](#) (NASDAQ:ALXN) today announced that the U.S. Food and Drug Administration (FDA) approved ULTOMIRIS® (ravulizumab-cwvz) for the treatment of atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA) for adult and pediatric (one month of age and older) patients. This is the first pediatric approval for ULTOMIRIS. Atypical HUS is an ultra-rare disease that can cause progressive injury to vital organs, primarily the kidneys, via damage to the walls of blood vessels and blood clots. Atypical HUS can cause sudden organ failure or a slow loss of function over time—potentially resulting in the need for a transplant, and in some cases, death.

“The primary approach to treatment is to prevent the body from attacking itself, through the inhibition of uncontrolled complement activation, referred to as C5 inhibition,” said Spero Cataland, M.D., Professor of Clinical Internal Medicine, Wexner Medical Center, The Ohio State University College of Medicine. “Clinical study results showed adult and pediatric patients had complete C5 inhibition following the first dose of ULTOMIRIS. C5 inhibition was sustained over time with only six or seven infusions a year in adults—and that is important to consider for my patients.”

Atypical HUS affects both adults and children and many patients present in critical condition, often requiring supportive care, including dialysis, in an intensive care unit. The prognosis of aHUS can be poor in many cases, so a timely and accurate diagnosis—in addition to treatment—is critical to improving patient outcomes.

“The consequences of uncontrolled complement activation, like organ failure and potentially death, create significant challenges and uncertainty for people and families facing aHUS,” said John Orloff, M.D., Executive Vice President and Head of Research and Development at Alexion. “Based on the Phase 3 data, which demonstrated clinically meaningful benefits in people with aHUS, we believe ULTOMIRIS has the potential to become the new standard of care for this devastating disease.”

The FDA approval is based on [data](#) from two global, single-arm open-label studies of ULTOMIRIS – one in adults and one in children, referred to as pediatrics in the study – with aHUS. The pediatric study is ongoing and a total of 14 out of 16 children were enrolled and included in the interim analysis. Efficacy evaluation of Complete TMA Response was defined by hematologic normalization parameters (platelet count and LDH) and improved kidney function (as measured by  $\geq 25$  percent improvement in serum creatinine from baseline). In the initial 26-week treatment periods, 54 percent of adults and 71 percent (interim data) of children demonstrated Complete TMA Response. Treatment with ULTOMIRIS resulted in reduced thrombocytopenia (low blood platelet count) in 84 percent of adults and 93 percent of children, reduced hemolysis (the destruction of red blood cells) in 77 percent of adults and 86 percent of children, and improved kidney function in 59 percent of adults and 79 percent (interim data) of children (for patients on dialysis at enrollment, baseline was established after they had come off dialysis).

The most frequently observed adverse reactions reported in these studies were upper respiratory tract infection, diarrhea, nausea, vomiting, headache, hypertension and pyrexia. Serious meningococcal infections have occurred in patients treated with ULTOMIRIS. To minimize the risk for patients, specific risk-mitigation plans, including a REMS, have been established for ULTOMIRIS.

Regulatory filings for marketing authorizations of ULTOMIRIS for the treatment of aHUS in the European Union (EU) and Japan are under review with regulators.

### About aHUS

Atypical hemolytic uremic syndrome (aHUS) is an ultra-rare disease that affects both children and adults and can lead to potentially irreversible damage to kidneys and other vital organs, sudden or progressive kidney failure (requiring dialysis or transplant) and premature death. aHUS is characterized by inflammation and the formation of blood clots in small blood vessels throughout the body (thrombotic microangiopathy [TMA]) mediated by chronic, uncontrolled activation of the complement system, which is part of the body’s immune system. TMA consists of reduced platelet count (thrombocytopenia), hemolytic anemia (as a result of hemolysis [destruction of red blood cells]) and acute kidney injury (AKI). If left untreated, significant proportions of adults (46 percent) and children (16 percent) can progress to end-stage renal disease (ESRD) or die during first clinical manifestations of aHUS despite supportive care, including plasma exchange or plasma infusion (PE/PI). One year following clinical manifestations, 56 percent of adults and 29 percent of children can progress to ESRD or die, if left untreated. Early and careful diagnosis of aHUS is critical, as many coexisting diseases and events are known or suspected to activate the complement cascade, and as patients may not necessarily present with the classic TMA triad of thrombocytopenia, hemolytic anemia and renal impairment or may have less severe renal involvement. Available tests can help distinguish aHUS from other hemolytic diseases with similar symptoms such as HUS caused by Shiga toxin-producing *Escherichia coli* (STEC-HUS) and thrombotic thrombocytopenic purpura (TTP).

### About ULTOMIRIS

ULTOMIRIS (ravulizumab-cwvz) is the first and only 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.

You can read more about the study results for this clinical program on [alexion.com](#).

## 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.

### 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 decided 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, and metabolic disorders. Alexion has been named to the *Forbes'* list of the World's Most Innovative Companies seven years in a row and is headquartered in Boston, Massachusetts' Innovation District. The company also 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](http://www.alexion.com).

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For patient or advocacy inquiries please contact [patientadvocacy@alexion.com](mailto:patientadvocacy@alexion.com).

### **Forward-Looking Statement**

This press release contains forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Alexion, including statements related to: the potential benefits of ULTOMIRIS as a treatment for patients with aHUS, the impact of aHUS on patients, the benefits of diagnosing aHUS in patients; the timing for regulatory filings for marketing authorizations of ULTOMIRIS for the treatment of aHUS in the EU and Japan; and that ULTOMIRIS can provide benefits for patients with aHUS. 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: the anticipated benefits of ULTOMIRIS for aHUS patients may not be realized; results of clinical trials may not be sufficient to satisfy any other regulatory authority in order to approve ULTOMIRIS as a treatment for aHUS or TMA (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 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 (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); 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 principal product (SOLIRIS); 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 failure of product candidates to obtain regulatory approval; 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 regarding products and product candidates; uncertainty of long-term success in developing, licensing or acquiring other product candidates or additional indications for existing products; inability to complete acquisitions or grow the product pipeline through acquisitions (including due to failure to obtain antitrust approvals); 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 and inter partes review petitions submitted 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; 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; the risk that estimates regarding the number of patients with PNH, aHUS, gMG, NMO, HPP and LAL-D and other indications we are pursuing are inaccurate; the risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructuring; risks related to the acquisition of Syntimmune and other companies and co-development efforts; 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 June 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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