



ULTOMIRIS® (ravulizumab) Receives Marketing Authorization from European Commission for Adults and Children with Atypical Hemolytic Uremic Syndrome (aHUS)

June 29, 2020

– ULTOMIRIS is the first and only long-acting C5 inhibitor for aHUS, administered every other month, reducing the treatment burden for adults and children –

– ULTOMIRIS has the potential to become the new standard of care in Europe for the treatment of aHUS –

– aHUS is an ultra-rare disease which may progressively damage the kidney and other organs^{1,2} –

BOSTON--(BUSINESS WIRE)--Jun. 29, 2020-- [Alexion Pharmaceuticals, Inc.](#) (NASDAQ:ALXN) today announced that the European Commission has approved ULTOMIRIS® (ravulizumab)—the first and only long-acting C5 complement inhibitor administered every eight weeks*—for the treatment of adults and children with a body weight of 10 kg or above with atypical hemolytic uremic syndrome (aHUS) who are complement inhibitor treatment-naïve or have received SOLIRIS® (eculizumab) for at least three months and have evidence of response to eculizumab.

“The consequences of aHUS are severe and potentially life-threatening, creating significant challenges and uncertainty for patients and their families. The goal of aHUS treatment is to prevent the body from attacking itself through the inhibition of uncontrolled C5 complement activation – a part of the body’s immune system,” said Prof. Dr. Hermann Haller, Clinic for Nephrology, University Hannover, Germany. “Clinical study results showed that both adults and children with aHUS had immediate and complete C5 inhibition following the first dose of ULTOMIRIS sustained for up to eight weeks. In addition to having demonstrated clinically meaningful benefits in people with aHUS, ULTOMIRIS provides greater freedom with significantly fewer infusions per year.”

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 affects both adults and children and many patients present in critical condition in the hospital setting, often requiring supportive care, including dialysis, in an intensive care unit. The prognosis of aHUS can be poor in many cases, with 56 percent of adults and 29 percent of children developing end-stage renal disease or dying within a year of diagnosis with supportive care alone,³ so a timely and accurate diagnosis – in addition to treatment – is critical to improving patient outcomes.

“At Alexion, our goal is to continue to improve the lives of people and families affected by aHUS and other serious rare diseases,” said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. “Treatment with ULTOMIRIS offers convenient eight-week dosing, which we believe is preferred by patients because it provides them with greater flexibility and improved quality of life, while also reducing the burden on healthcare systems that currently face significant strain in many countries. Today’s marketing authorization marks an important step in our efforts to establish ULTOMIRIS as the new standard of care for the aHUS patient community.”

The European Commission 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. Both studies are ongoing. A total of 18 out of 21 complement inhibitor treatment-naïve children and 56 out of 58 complement inhibitor treatment-naïve adults were enrolled and included in the interim analysis. Efficacy evaluation of Complete TMA Response was defined by normalization of hematologic parameters (platelet count and LDH) and improved kidney function (as measured by ≥ 25 percent improvement in serum creatinine from baseline). In the initial 26-week treatment periods, 54 percent of adults and 77.8 percent (interim data) of children demonstrated Complete TMA Response. Treatment with ULTOMIRIS resulted in normalization of platelet count in 84 percent of adults and 94 percent of children, normalization of LDH (marker of hemolysis) in 77 percent of adults and 90 percent of children, and improved kidney function in 59 percent of adults and 83 percent (interim data) of children (for patients on dialysis at enrollment, baseline was established after they had come off dialysis). In the 52-week follow-up period, 4 additional adult patients and 3 pediatric patients had a Complete TMA Response that was confirmed after the 26-week Initial Evaluation Period resulting in an overall Complete TMA Response of 61 percent in adults and 94 percent in children (interim data). Treatment with ULTOMIRIS resulted in normalization of platelet count in 86 percent of adults and 94 percent of children, normalization of LDH (marker of hemolysis) in 84 percent of adults and 94 percent of children, and improved kidney function in 63 percent of adults and 94 percent (interim data) of children (for patients on dialysis at enrollment, baseline was established after they had come off dialysis). A second cohort of 10 pediatric patients who were SOLIRIS-experienced were included in the pediatric study, demonstrating that switching to ULTOMIRIS maintained disease control as evidenced by stable hematologic and renal parameters, with no apparent impact on safety.

The most frequently observed adverse reactions reported in these studies were upper respiratory tract infection, diarrhea, nausea, fatigue, headache, nasopharyngitis, and pyrexia. Serious meningococcal infections have occurred in patients treated with ULTOMIRIS, however in aHUS studies, no meningococcal infections occurred in the 89 patients receiving treatment with ULTOMIRIS. To minimize the risk for patients, specific risk-mitigation plans, including a Risk Management Plan, have been established for ULTOMIRIS.

The U.S. Food and Drug Administration (FDA) approved ULTOMIRIS for the treatment of aHUS to inhibit TMA for adult and pediatric (one month of age and older) patients in [October 2019](#). A regulatory filing for marketing authorization of ULTOMIRIS for the treatment of aHUS in Japan is currently under review. ULTOMIRIS is also approved for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH) in the U.S and Japan, and in the EU as a treatment for adult patients with PNH with hemolysis with clinical symptoms indicative of high disease activity and also for adult patients who are clinically stable after having been treated with eculizumab for at least the past six months.

* Starting two weeks after the loading dose, maintenance doses are administered once every four or eight weeks (depending on body weight)

About Atypical Hemolytic Uremic Syndrome (aHUS)

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 occurs when the complement system—a part of the body's immune system—over-responds, leading the body to attack its own healthy cells. 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. 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. Available tests can help distinguish aHUS from other hemolytic diseases with similar symptoms.

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 every four weeks for pediatric patients less than 20 kg, following a loading dose. ULTOMIRIS is approved in the United States (U.S.), European Union (EU) and Japan as a treatment for adults with paroxysmal nocturnal hemoglobinuria (PNH) and in the U.S. for atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA) in adult and pediatric (one month of age and older) patients. To learn more about the regulatory status of ULTOMIRIS in the countries that we serve, please visit www.alexion.com.

U.S. INDICATIONS & IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS (ravulizumab-cwvz) 300 mg / 30 mL injection for intravenous use

U.S. 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.

U.S. 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 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 and devastating diseases through the discovery, development and commercialization of life-changing medicines. 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 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 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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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: treatment with ULTOMIRIS will offer convenient eight-week dosing without compromising efficacy or safety; treatment with ULTOMIRIS is preferred by patients because it provides them with greater flexibility and improved quality of life, while also reducing the burden on healthcare systems; the consequences of aHUS create significant challenges and uncertainty for patients and their families; timely and accurate diagnosis of aHUS – in addition to treatment – is critical to improving patient outcomes; the Company's goal is to continue to improve the lives of people and families affected by aHUS and other serious rare diseases; the marketing authorization marks an important step in our efforts to establish ULTOMIRIS as the new standard of care for the aHUS patient community; and ULTOMIRIS has the potential to become the new standard of care in Europe for the treatment of aHUS; the anticipated benefits of ULTOMIRIS as a treatment 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 (and the results of the clinical trials may not be indicative of the results realized by patients); use of ULTOMIRIS does not ultimately provide comparable efficacy and safety to patients using the therapy; results in clinical trials may not be indicative of results from later stage or larger clinical trials (or in broader patient populations after the product is approved for use by regulatory agencies); ULTOMIRIS may not be adopted by physicians, patients and payers as a treatment for aHUS (and may not be accepted as the standard of care); 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 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 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 the European Commission and other 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); 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 COVID-19; uncertainties surrounding legal proceedings, company investigations and government investigations, including investigations of Alexion by the U.S. Securities and Exchange Commission; 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 risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructuring; risks related to the pending acquisition of Portola Pharmaceuticals, Inc., the acquisition of Achillion 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 period ended March 31, 2020 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.

References:

1. Laurence J. Atypical hemolytic uremic syndrome (aHUS): making the diagnosis. *Clin Adv Hematol Oncol*. 2012;10(suppl 17):1-12.
2. Campistol JM, Arias M, Ariceta G, et al. An update for atypical haemolytic uraemic syndrome: diagnosis and treatment. *Nefrologia*. 2013 Jan 18;33(1): 27-45.
3. Fremeaux -Bacchi, V, et al. Genetics and outcomes of atypical HUS in Children and Adults: A Nationwide French Series Comparing Children and Adults. *Clin J Am Soc Nephrol*. April 2013, 8 (4) 554-562; DOI: <https://doi.org/10.2215/CJN.04760512>

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