



Alexion Provides Update on Phase 3 Study of ULTOMIRIS® (ravulizumab-cwvz) in Hospitalized Patients with Severe COVID-19

January 13, 2021

- Independent data monitoring committee recommends pausing study enrollment due to lack of efficacy in pre-specified interim analysis –
- Company will conduct further analysis of trial data to determine next steps –
- No new safety findings were observed for ULTOMIRIS use in COVID-19 –

BOSTON--(BUSINESS WIRE)--Jan. 13, 2021-- [Alexion Pharmaceuticals, Inc.](#) (NASDAQ:ALXN) today announced the decision to pause further enrollment in the global Phase 3 study of ULTOMIRIS® (ravulizumab-cwvz) in adults with severe COVID-19 requiring mechanical ventilation. This decision is based on the recommendation of an independent data monitoring committee (IDMC), following their review of data from a pre-specified interim analysis. The IDMC recommended that additional enrollment be paused, pending further analysis of the data, due to lack of efficacy when ULTOMIRIS was added to best supportive care, compared to best supportive care alone. There were no new safety findings observed. The study will continue for patients already enrolled, including completion of all study visits and planned ULTOMIRIS dosing according to the study protocol.

“We would like to thank the patients and their families, as well as investigators and healthcare professionals, who were essential to this study. We greatly value their contributions to help investigate potential ways to address this devastating pandemic,” said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. “While initial anecdotal reports from compassionate use cases were promising, these results demonstrate the importance of conducting controlled clinical trials to fully evaluate the potential of new treatment approaches and generate the necessary evidence to make informed decisions. We are disappointed in this initial outcome, but plan to further analyze the data to identify potential subgroups who may benefit and to determine next steps. In addition, we remain fully committed to our efforts to serve the rare disease community and to continuing to provide ULTOMIRIS to the patients who currently rely on it.”

The IDMC’s recommendation was based on a pre-planned interim analysis of the primary endpoint – survival at Day 29 – once 122 patients completed the 29-day primary evaluation period. No secondary endpoints were analyzed as part of the interim analysis.

In the UK, the TACTIC-R platform study led by Cambridge University Hospitals NHS Foundation Trust, which includes an ULTOMIRIS cohort, is evaluating the potential of earlier immune modulatory treatment (hospitalized patients not requiring mechanical ventilation) in preventing progression of the virus, including reducing the need for ICU admission and ventilation. This independent study remains ongoing.

About ULTOMIRIS® (ravulizumab-cwvz)

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.), European Union (EU) and Japan as a treatment for adults with paroxysmal nocturnal hemoglobinuria (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.

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

INDICATIONS

What is ULTOMIRIS?

ULTOMIRIS is a prescription medicine used to treat:

- adults 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 with PNH.

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 *Haemophilus 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, pain with the infusion, 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 infection and headache.

The most common side effects of ULTOMIRIS in people with aHUS are upper respiratory 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 the core therapeutic areas of hematology, nephrology, neurology, metabolic disorders, cardiology and ophthalmology. 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 may include statements that are or may be deemed to be forward-looking statements. These forward-looking statements may be identified by the use of forward-looking terminology, including the terms "believes", "estimates", "envisages", "plans", "projects", "anticipates", "targets", "aims", "expects", "intends", "may", "will" or "should" or, in each case, their negative or other variations or comparable terminology, or by discussions of strategy, plans, objectives, goals, future events or intentions and include, but are not limited to the plans of Alexion with respect to ULTOMIRIS as a potential treatment for severe COVID-19 patients. Economic, competitive, governmental, technological and other factors that may affect Alexion's operations are discussed in the section entitled "Risk Factors," Alexion's Quarterly Report on Form 10-Q for the Period ended 30 September 2020, as amended by any subsequent filings made with the SEC. These forward-looking statements include all matters that are not historical facts and involve predictions. Forward-looking statements may and often do differ materially from actual results. Any forward-looking statements reflect Alexion's current views with respect to future events and are subject to risks relating to future events and other risks, uncertainties and assumptions relating to Alexion's results of operations, financial position, liquidity, prospects, growth or strategies and the industries in which they operate. Forward-looking statements speak only as of the date they are made and cannot be relied upon as a guide to future performance. Save as required by law or regulation, Alexion disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements in this press release that may occur due to any change in its expectations or to reflect events or circumstances after the date of this press release.

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