ULTOMIRIS® (ravulizumab-cwvz) met primary endpoint in CHAMPION-NMOSD Phase III trial in adults with neuromyelitis optica spectrum disorder

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Zero adjudicated relapses observed among ULTOMIRIS patients over a median treatment duration of 73 weeks

WILMINGTON, Del., May 5, 2022 – Positive high-level results from the open-label Phase III CHAMPION-NMOSD trial showed that ULTOMIRIS® (ravulizumab-cwvz) achieved a statistically significant and clinically meaningful reduction in the risk of relapse in adults with anti-aquaporin-4 (AQP4) antibody-positive (Ab+) neuromyelitis optica spectrum disorder (NMOSD) compared to the external placebo arm from the pivotal SOLIRIS® PREVENT clinical trial.

ULTOMIRIS, the first and only long-acting C5 complement inhibitor, met the primary endpoint of time to first on-trial relapse, as confirmed by an independent adjudication committee. Notably, no relapse was observed in 58 patients over a median treatment duration of 73 weeks.

NMOSD is a rare and devastating autoimmune disease that affects the central nervous system (CNS), including the spine and optic nerves.1-3 Most people living with NMOSD often experience unpredictable relapses, a new onset of neurologic symptoms or worsening of existing neurologic symptoms, also referred to as attacks, which tend to be severe and recurrent and may result in permanent disability.4-6

Sean J. Pittock, MD, Director of Mayo Clinic's Center for Multiple Sclerosis and Autoimmune Neurology and of Mayo's Neuroimmunology Laboratory and lead primary investigator in the CHAMPION-NMOSD trial, said: “Every NMOSD relapse can have debilitating and irreversible consequences, so reducing relapses is critical. Patients on ULTOMIRIS remained relapse free over a median treatment duration of 73 weeks in the trial.”

Marc Dunoyer, Chief Executive Officer, Alexion, said: “SOLIRIS established the role of complement inhibition in preventing relapses in NMOSD, and with ULTOMIRIS, we continue to innovate for patients with a more convenient every eight-week dosing schedule. These trial results show that ULTOMIRIS may help patients move towards eliminating relapses, which is an important advancement in the treatment of NMOSD.”

The safety and tolerability of ULTOMIRIS in the Champion-NMOSD trial were consistent with previous clinical studies and other approved indications. Fifty-six patients are continuing to receive treatment in a long-term extension period, which is ongoing.

The data will be presented at a forthcoming medical meeting and submitted to global health authorities as rapidly as possible to bring forward ULTOMIRIS to the NMOSD community.

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

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).
- adults with a disease called generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.

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, tiredness, feeling faint, discomfort in your arms or legs, or bad taste. 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.

The most common side effects of ULTOMIRIS in people with gMG are diarrhea and upper respiratory tract infection.

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.

Notes

NMOSD

NMOSD is a rare disease in which the immune system is inappropriately activated to target healthy tissues and cells in the CNS.[1,2] Approximately three-quarters of people with NMOSD are anti-AQP4 Ab+, meaning they produce antibodies that bind to a specific protein, aquaporin-4 (AQP4).[7] This binding can inappropriately activate the complement system, which is part of the immune system and is essential to the body's defense against infection, to destroy cells in the optic nerve, spinal cord and brain. [1,8,9]

It most commonly affects women and begins in the mid-30s. Men and children may also develop NMOSD, but it is even more rare.[10,11] People with NMOSD may experience vision problems, intense pain, loss of bladder/bowel function, abnormal skin sensations (eg, tingling, prickling or sensitivity to heat/cold) and impact on coordination and/or movement.[3-5,12,13] Most people living with NMOSD experience unpredictable relapses, also known as attacks. Each relapse can result in cumulative disability including vision loss, paralysis and sometimes premature death.[4-6] NMOSD is a distinct disease from other CNS diseases, including multiple sclerosis. The journey to diagnosis can be long, with the disease sometimes misdiagnosed.[14-16]

CHAMPION-NMOSD

CHAMPION-NMOSD is a global Phase III, open-label, multicenter trial evaluating the safety and efficacy of ULTOMIRIS in adults with NMOSD. The trial enrolled 58 patients across North America, Europe, Asia-Pacific and Japan. Participants were required to have a confirmed NMOSD diagnosis with a positive anti-AQP4 antibody test, at least one attack or relapse in the twelve months prior to the screening visit, an Expanded Disability Status Scale Score of 7 or less and body weight of at least 40 kilograms at trial entry. Participants could stay on stable supportive immunosuppressive therapy for the duration of the trial.[17]

Due to the potential long-term functional impact of NMOSD relapses, a direct placebo comparator arm was precluded for ethical reasons. The active treatment was compared to an external placebo arm from the pivotal SOLIRIS PREVENT clinical trial.

Over a median treatment duration of 73 weeks, all enrolled patients received a single weight-based loading dose of ULTOMIRIS on Day 1, followed by regular weight-based maintenance dosing beginning on Day 15, every eight weeks. The primary endpoint was time to first on-trial relapse, as confirmed by an independent adjudication committee. The end of the primary treatment period could have occurred either when all patients completed or discontinued prior to the Week 26 visit and two or more adjudicated relapses were observed, or when all patients completed or discontinued prior to the Week 50 visit if fewer than two adjudicated relapses were observed. In the trial, there were zero adjudicated relapses so the end of the primary treatment period occurred when the last enrolled participant completed the 50 week visit.

Patients who completed the primary treatment period were eligible to continue into a long-term extension period, which is ongoing.

ULTOMIRIS

ULTOMIRIS (ravulizumab-cwvz), the first and only long-acting C5 complement inhibitor, offers immediate, complete and sustained complement inhibition. 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 in adult patients, following a loading dose.

ULTOMIRIS is approved in the US for the treatment of certain adults with generalized myasthenia gravis.

ULTOMIRIS is also approved in the US, EU and Japan for the treatment of certain adults and children with paroxysmal nocturnal hemoglobinuria.

Additionally, ULTOMIRIS is approved in the US, EU and Japan for certain adults and children with atypical hemolytic uremic syndrome to inhibit complement-mediated thrombotic microangiopathy.

As part of a broad development program, ULTOMIRIS is being assessed for the treatment of additional hematology and neurology indications.

Alexion

Alexion, AstraZeneca Rare Disease, is the group within AstraZeneca focused on rare diseases, created following the 2021 acquisition of Alexion Pharmaceuticals, Inc. As a leader in rare diseases for nearly 30 years, Alexion is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialization of life-changing medicines. 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 and ophthalmology. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in more than 50 countries. For more information, please visit www.alexion.com.

About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialization of prescription medicines in Oncology, Rare Diseases and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca-us.com and follow us on Twitter @AstraZenecaUS.

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Dr. Pittock has provided consulting services to Alexion.