Danicopan (ALXN2040) add-on to ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab) met primary endpoint in ALPHA Phase III trial for patients with paroxysmal nocturnal hemoglobinuria who experience clinically significant extravascular hemolysis

September 16, 2022

Interim results demonstrate statistically significant improvement compared to placebo in hemoglobin levels from baseline to week 12

WILMINGTON, Del., September 16, 2022 – A prespecified interim analysis of the ALPHA Phase III trial evaluating danicopan (ALXN2040), an investigational, oral factor D inhibitor, as an add-on to C5 inhibitor therapy ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab) showed positive high-level results in patients with paroxysmal nocturnal hemoglobinuria (PNH) who experience clinically significant extravascular hemolysis (EVH).

The trial met its primary endpoint of change in hemoglobin from baseline at 12 weeks and key secondary endpoints, including transfusion avoidance and change in Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue score. Danicopan plus ULTOMIRIS or SOLIRIS demonstrated superiority compared to placebo plus ULTOMIRIS or SOLIRIS for this specific patient population, with statistically significant and clinically meaningful improvements in hemoglobin levels, transfusion avoidance and FACIT Fatigue scores from baseline.

PNH is a rare and severe blood disorder characterized by the destruction of red blood cells, known as intravascular hemolysis (IVH), and white blood cell and platelet activation that can cause thrombosis (blood clots) and result in organ damage and potentially premature death.1-3

Marc Dunoyer, Chief Executive Officer, Alexion, said: “Alexion has relentlessly innovated for the PNH community, pioneering with SOLIRIS, the first treatment for PNH, and establishing ULTOMIRIS as a standard of care. We are proud of our continued innovation to advance new ways of targeting the complement cascade to help address the needs of patients living with this debilitating disease. These are the first positive Phase III results for an oral factor D inhibitor and demonstrate the potential for danicopan add-on therapy to improve signs and symptoms and reduce the need for transfusions for the limited proportion of people living with PNH who experience clinically significant EVH.”

Professor Jong-Wook Lee, MD, PhD, Department of Hematology at Seoul St. Mary's Hospital of The Catholic University of Korea, and investigator in the ALPHA trial, said: “C5 inhibitors are a proven treatment option for patients living with PNH, yet a small percentage may continue to experience anemia and burden of transfusion due to clinically significant EVH, however it is not life-threatening. These data show that danicopan has the potential to resolve clinically significant EVH while allowing patients to remain on standard of care treatment with ULTOMIRIS or SOLIRIS.”

Danicopan was generally well tolerated and there were no clinically meaningful differences in safety results observed between the danicopan plus C5 inhibitor group and control group.

Alexion, AstraZeneca Rare Disease, will present these data at a forthcoming medical meeting and intends to proceed with regulatory submissions in the coming months.

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.

INDICATIONS & IMPORTANT SAFETY INFORMATION FOR SOLIRIS® (eculizumab) [injection for intravenous use 300mg/30mL vial]

What is SOLIRIS?
SOLIRIS is a prescription medicine used to treat:

- patients with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH).
- adults and children with a disease called atypical Hemolytic Uremic Syndrome (aHUS). SOLIRIS is not for use 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.
- adults with a disease called neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive.

It is not known if SOLIRIS is safe and effective in children with PNH, gMG, or NMOSD.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about SOLIRIS?
SOLIRIS is a medicine that affects your immune system and can lower the ability of your immune system to fight infections.

- **SOLIRIS 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.**
- You must receive meningococcal vaccines at least 2 weeks before your first dose of SOLIRIS if you are not vaccinated.
- If your doctor decided that urgent treatment with SOLIRIS is needed, you should receive meningococcal vaccination as soon as possible.
- If you have not been vaccinated and SOLIRIS therapy must be initiated immediately, you should also receive 2 weeks of antibiotics with your vaccinations.
- If you had a meningococcal vaccine in the past, you might need additional vaccination. Your doctor will decide if you need additional vaccination.
- 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 3 months after your last SOLIRIS dose. It is important to show this card to any doctor or nurse to help them diagnose and treat you quickly.

SOLIRIS is only available through a program called the SOLIRIS REMS. Before you can receive SOLIRIS, your doctor must enroll in the SOLIRIS 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 the 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.

SOLIRIS 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 SOLIRIS. Certain people may be at risk of serious infections with gonorrhea. Certain fungal infections (Aspergillus) may occur if you take SOLIRIS and have a weak immune system or a low white blood cell count.

Who should not receive SOLIRIS?
Do not receive SOLIRIS if you have a meningococcal infection or have not been vaccinated against meningitis infection unless your doctor decides that urgent treatment with SOLIRIS is needed.

Before you receive SOLIRIS, 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 SOLIRIS will harm your unborn baby or if it passes into your breast milk.

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. It is important that you have all recommended vaccinations before you start SOLIRIS, receive 2 weeks of antibiotics if you immediately start SOLIRIS, and stay up-to-date with all recommended vaccinations during treatment with SOLIRIS.

If you have PNH, your doctor will need to monitor you closely for at least 8 weeks after stopping SOLIRIS. Stopping treatment with SOLIRIS 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 the number of your red blood cell count, drop in your platelet count, confusion, kidney problems, blood clots, difficulty breathing, and chest pain.

If you have aHUS, your doctor will need to monitor you closely during and for at least 12 weeks after stopping treatment for signs of worsening aHUS symptoms or problems related to abnormal clotting (thrombotic microangiopathy). Symptoms or problems that can happen with abnormal clotting may include: stroke, confusion, seizure, chest pain (angina), difficulty breathing, kidney problems, swelling in arms or legs, and a drop in your platelet count.

What are the possible side effects of SOLIRIS?

SOLIRIS can cause serious side effects including serious allergic reactions. Tell your doctor or nurse right away if you get any of these symptoms during your SOLIRIS infusion: chest pain; trouble breathing or shortness of breath; swelling of your face, tongue, or throat; and feel faint or pass out. If you have an allergic reaction to SOLIRIS, your doctor may need to infuse SOLIRIS more slowly, or stop SOLIRIS.

The most common side effects in people with PNH treated with SOLIRIS include: headache, pain or swelling of your nose or throat (nasopharyngitis), back pain, and nausea.

The most common side effects in people with aHUS treated with SOLIRIS include: headache, diarrhea, high blood pressure (hypertension), common cold (upper respiratory infection), stomach-area (abdominal) pain, vomiting, pain or swelling of your nose or throat (nasopharyngitis), low red blood cell count (anemia), cough, swelling of legs or feet (peripheral edema), nausea, urinary tract infections, and fever.

The most common side effects in people with gMG treated with SOLIRIS include: muscle and joint (musculoskeletal) pain.

The most common side effects in people with NMOSD treated with SOLIRIS include: common cold (upper respiratory infection); pain or swelling of your nose or throat (nasopharyngitis); diarrhea; back pain; dizziness; flu-like symptoms (influenza), including fever, headache, tiredness, cough, sore throat, and body aches; joint pain (arthralgia); throat irritation (pharyngitis); and bruising (contusion).

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 SOLIRIS. For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch, or call 1-800-FDA-1088.

Please see the full Prescribing Information and Medication Guide for SOLIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections.

Notes

PNH

PNH is a rare, chronic, progressive and potentially life-threatening blood disorder. It is characterized by red blood cell destruction within blood vessels (also known as intravascular hemolysis) and white blood cell and platelet activation, which can result in thrombosis (blood clots).[1-3]

PNH is caused by an acquired genetic mutation that may happen any time after birth and results in the production of abnormal blood cells that are missing important protective blood cell surface proteins. These missing proteins enable the complement system, which is part of the immune system and is essential to the body's defense against infection, to 'attack' and destroy or activate these abnormal blood cells.1 Living with PNH can be debilitating, and signs and symptoms may include blood clots, abdominal pain, difficulty swallowing, erectile dysfunction, shortness of breath, excessive fatigue, anemia and dark-colored urine.[1,4,5]

Clinically Significant EVH

EVH, the removal of red blood cells outside of the blood vessels, can sometimes occur in PNH patients who are treated with C5 inhibitors. Since C5 inhibition enables PNH red blood cells to survive and circulate, EVH may occur when these now surviving PNH red blood cells are marked by proteins in the complement system for removal by the spleen and liver.1,3,6 PNH patients with EVH may continue to experience anemia, which can have various causes, and may require blood transfusions.[6] A small subset of people living with PNH who are treated with a C5 inhibitor experience clinically significant EVH, which can result in continued symptoms of anemia and require blood transfusions.

ALPHA

ALPHA is a pivotal, global Phase III trial designed to evaluate the efficacy of danicopan as an add-on to C5 inhibitor therapy ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab) in patients with PNH who experience clinically significant EVH. In the double-blind, placebo controlled, multiple-dose trial, patients were enrolled and randomized to receive danicopan or placebo (2:1) in addition to their ongoing C5 inhibitor therapy for 12 weeks. Prespecified interim analysis for efficacy was planned once 75 percent (N~63) of participants completed 12 weeks of treatment period 1. At 12 weeks, patients on placebo plus C5 inhibitor are switched to danicopan plus a C5 inhibitor and patients on danicopan plus a C5 inhibitor remain on treatment for an additional 12 weeks.

Patients who complete both treatment periods (24 weeks) have the option to participate in a long-term extension period and continue to receive danicopan in addition to C5

inhibitor therapy.

Danicopan (ALXN2040)

Danicopan is an investigational oral medicine in development as an add-on to C5 inhibitor therapy ULTOMIRIS® (ravulizumab-cwvz) or SOLIRIS® (eculizumab) for patients with PNH who experience clinically significant EVH. It is designed to selectively inhibit factor D, a complement system protein that plays a key role in the amplification of the complement system response. Danicopan has been granted Breakthrough Therapy designation by the US Food and Drug Administration and PRIority MEdicines (PRIME) status by the European Medicines Agency. Danicopan has also been granted Orphan Drug Designation in the US and orphan designation in the EU for the treatment of PNH. Alexion is also evaluating danicopan as a potential monotherapy for geographic atrophy in a Phase II clinical trial.

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 and Japan for the treatment of certain adults with gMG.

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

Additionally, ULTOMIRIS is approved in the US, EU and Japan for certain adults and children with aHUS 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.

SOLIRIS

SOLIRIS (eculizumab) is a first-in-class 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 terminal complement cascade over-responds, leading the body to attack its own healthy cells. SOLIRIS is administered intravenously every two weeks, following an introductory dosing period.

SOLIRIS is approved in the US, EU and Japan for the treatment of PNH, aHUS, certain adults with gMG and certain adults with NMOSD.

SOLIRIS is not indicated for the treatment of patients with STEC-HUS.

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 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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