



## Alexion Announces Plans to Initiate Phase 3 Study of ULTOMIRIS® (ravulizumab-cwvz) in Hospitalized Patients with Severe COVID-19

April 20, 2020

- Global study to enroll approximately 270 adults with COVID-19 and severe pneumonia or acute respiratory distress syndrome -

- Company maintains commitment to supplying its medicines to patients for currently approved indications -

BOSTON--(BUSINESS WIRE)--Apr. 20, 2020-- [Alexion Pharmaceuticals, Inc.](https://www.alexion.com) (NASDAQ:ALXN) today announced plans to initiate a global Phase 3 study to investigate ULTOMIRIS® (ravulizumab-cwvz) in a subset of adults with COVID-19 – those who are hospitalized with severe pneumonia or acute respiratory distress syndrome (ARDS). The study is expected to enroll approximately 270 patients across countries with high numbers of diagnosed cases, beginning in May, and will evaluate the impact of ULTOMIRIS, a biologic medicine, on survival, duration of mechanical ventilation, and hospital stay compared to best supportive care. This follows the U.S. Food and Drug Administration's (FDA) rapid review and acceptance of Alexion's investigational new drug (IND) application for ULTOMIRIS for severe COVID-19.

"Alexion has been in close contact with physicians and global health authorities in an effort to rapidly evaluate the potential of C5 inhibition in treating patients with severe COVID-19," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "Based on early anecdotal information available from compassionate use cases in multiple countries, we are launching a controlled clinical trial to evaluate the potential of ULTOMIRIS in mitigating the severe pneumonia and lung injury caused by the virus. As we move quickly to initiate this program, we also remain committed to serving the patients who currently rely on our medicines and providing continuous supply to these patients."

The decision to begin this trial is based on a) published preclinical data suggesting that inhibition of terminal complement can lower cytokine and chemokine levels and significantly reduce lung inflammation and pathology in animal models of viral pneumonia<sup>1</sup>, and b) elevated complement biomarkers and promising preliminary clinical evidence from patients who have accessed SOLIRIS® (eculizumab) through our compassionate use program, which suggests that complement inhibition may improve coronaviral-mediated lung injury.

Independent investigators have expressed interest in studying the potential of C5 inhibition in severe COVID-19 pneumonia, and we are aware of several ongoing or planned independent studies and anecdotal results from the use of our C5 inhibitors in patients with COVID-19. While these healthcare professionals continue to aggregate data regarding the potential of terminal complement inhibition in COVID-19 pneumonia from the approximately 100 patients who have been treated so far, Alexion believes that the outcomes reported to date warrant conducting a controlled clinical program to explore the impact of C5 inhibition with ULTOMIRIS and establish clinical evidence supporting the role of terminal complement in coronaviral pneumonia. We believe ULTOMIRIS represents the future of C5 inhibition, with its weight-based dosing, reduced burden on hospital systems due to less frequent dosing and it can be manufactured at a higher capacity, providing the opportunity to better meet future supply demands.

For additional information on Alexion's ongoing efforts related to COVID-19, please visit: <https://alexion.com/our-commitment/covid-19>.

### About the Phase 3 Study

The Phase 3 open-label, randomized, controlled study is designed to evaluate the safety and efficacy of ULTOMIRIS in approximately 270 adults hospitalized with COVID-19 and severe pneumonia, acute lung injury or acute respiratory distress syndrome (ARDS). Study participants will be randomized 2:1 to receive ULTOMIRIS or best supportive care. The primary endpoint is survival at Day 29. Secondary endpoints will assess the need for mechanical ventilation, oxygenation, duration of ICU stay and hospitalization, and safety, among others.

Patients in the ULTOMIRIS arm will receive a weight-based loading dose of ULTOMIRIS on Day 1 (2400mg for patients weighing 40-60kg, 2700mg for 60-100kg, or 3000mg for ≥100kg). Follow-up dosing on Days 5 and 10 will also be weight-based; patients weighing 40 to 60kg will receive 600mg of ULTOMIRIS and patients weighing 60kg or more will receive 900mg of ULTOMIRIS. On Day 15, all patients will receive 900mg of ULTOMIRIS. All patients will continue to receive medications, therapies, and interventions per standard hospital treatment protocols for the duration of the study. Following the 4-week treatment period, there will be safety follow-up monitoring for three months.

### Expanded Access Programs

In recognition of the urgent needs of some patients and in order to streamline the emergency access process, Alexion has opened emergency Expanded Access Programs (EAP) in the U.S. and France for SOLIRIS in severe COVID-19 pneumonia. All requests for a hospital to be included in the EAP must be made by a treating physician and can be submitted to [covid.requests@alexion.com](mailto:covid.requests@alexion.com).

### Access & Supply Considerations

Alexion's focus has always been on developing transformative medicines for patients with rare and ultra-rare diseases that typically affect several hundred to a few thousand patients worldwide. Like all of our medicines, ULTOMIRIS is a biologic medicine, which are very large complex molecules made up of genetically engineered proteins that are manufactured in living cells through a highly complicated process that requires significant time, expertise and precision. During this global health crisis, we have taken proactive measures that are designed to mitigate the risk of potential supply interruptions, and we strive to maintain sufficient inventory levels to continue serving current and new patients receiving our medicines for approved rare and ultra-rare indications as well as those participating in ongoing clinical trials.

We recognize that, should the role of C5 in treating severe respiratory complications of COVID-19 be demonstrated in a controlled clinical trial, there is the potential for significantly increased demand for our C5 inhibitors. We have taken steps to significantly increase future supply as part of our efforts

to prepare for this and other potential scenarios that may arise so that we are ready to support access and the anticipated increased supply demand. In the meantime, Alexion will continue to monitor and manage the production of ULTOMIRIS, appropriately taking into consideration the needs of current and new patients, required inventory levels, anticipated potential supply needs related to COVID-19 and the time-intensive and complex manufacturing process to produce monoclonal antibodies while maintaining the company's rigorous quality standards.

### **About ULTOMIRIS<sup>®</sup> (ravulizumab-cwvz)**

ULTOMIRIS<sup>®</sup> (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. For currently approved indications, 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.

### **INDICATIONS & IMPORTANT SAFETY INFORMATION FOR ULTOMIRIS<sup>®</sup> (ravulizumab-cwvz) AND SOLIRIS<sup>®</sup> (eculizumab)**

#### **INDICATIONS**

ULTOMIRIS and SOLIRIS are prescription medicines called monoclonal antibodies. ULTOMIRIS and SOLIRIS are used to treat adults with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH). ULTOMIRIS and SOLIRIS are also used to treat adults and children with a disease called atypical Hemolytic Uremic Syndrome (aHUS). Neither ULTOMIRIS nor SOLIRIS is for use in treating people with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

In addition, SOLIRIS is used to treat adults with a disease called generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive. SOLIRIS is also used to treat adults with a disease called neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive.

It is not known if ULTOMIRIS is safe and effective in children with PNH or in children younger than one month of age in aHUS. It is also not known if SOLIRIS is safe and effective in children with PNH, gMG, or NMOSD.

#### **IMPORTANT SAFETY INFORMATION**

ULTOMIRIS and SOLIRIS are medicines that affect the immune system. These medicines can lower the ability of the immune system to fight infections. Both medicines increase 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 two weeks before the first dose of ULTOMIRIS or SOLIRIS if the patient has not already had this vaccine. If the patient's doctor decided that urgent treatment is needed, meningococcal vaccination should be administered as soon as possible. If the patient has not been vaccinated and therapy must be initiated immediately, two weeks of antibiotics should also be administered with the vaccinations. If the patient had a meningococcal vaccine in the past, additional vaccination might be needed before starting ULTOMIRIS or SOLIRIS. Patients should ask their doctor if an additional meningococcal vaccination is needed. Meningococcal vaccines reduce the risk of meningococcal infection but do not prevent all meningococcal infections. Patients should be instructed to call their 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. The doctor will provide a Patient Safety Card about the risk of meningococcal infection. This card must be carried at all times during treatment and for 8 months after the last ULTOMIRIS dose or 3 months after the last SOLIRIS dose.

Before a patient can receive ULTOMIRIS or SOLIRIS, their doctor must: enroll in the corresponding [ULTOMIRIS REMS](#) or [SOLIRIS REMS](#) program; counsel the patient about the risk of meningococcal infection; give the patient information and a Patient Safety Card about the symptoms and risk of meningococcal infection (as discussed above); and make sure that the patient is vaccinated with a meningococcal vaccine.

ULTOMIRIS and SOLIRIS may also increase the risk of other types of serious infections. Patients should talk to their doctor right away if they have any new signs or symptoms of infection.

Patients must not receive ULTOMIRIS or SOLIRIS if they have a meningococcal infection, or if they have not been vaccinated against meningococcal infection, unless their doctor decides that urgent treatment is needed.

Before a patient receives ULTOMIRIS or SOLIRIS, they should tell their doctor about all of their medical conditions, including if they: 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 or SOLIRIS will harm an unborn baby or if these medicines pass into the breast milk.

Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ULTOMIRIS and SOLIRIS can affect how other medicines work, causing side effects.

For patients with PNH, the doctor will need to monitor the patient closely for at least 16 weeks after stopping ULTOMIRIS or 8 weeks after stopping SOLIRIS. Stopping treatment with these medicines may cause breakdown of the red blood cells due to PNH. Symptoms or problems that can happen due to red blood cell breakdown include: a drop in 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.

For patients with aHUS, the doctor will need to monitor closely during and for at least 12 months after stopping ULTOMIRIS, or 12 weeks after stopping SOLIRIS, for signs of worsening aHUS symptoms or problems related to abnormal clotting and breakdown of 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.

ULTOMIRIS can cause serious side effects including infusion reactions. 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. Patients should tell their doctor or nurse right away if they develop these symptoms, or any other symptoms during their ULTOMIRIS infusion that may mean they are 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.

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.

SOLIRIS can cause serious side effects including serious allergic reactions. Serious allergic reactions can happen during the SOLIRIS infusion. Patients should tell their doctor or nurse right away if they get any of these symptoms during the SOLIRIS infusion: chest pain, trouble breathing or shortness of breath, swelling of the face, tongue, or throat, and feeling faint or pass out. If a patient has an allergic reaction to SOLIRIS, the 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 the 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 the 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 the 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 ULTOMIRIS or SOLIRIS. For more information, ask your doctor or pharmacist. Call your doctor right away if you miss an ULTOMIRIS or SOLIRIS infusion or for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please refer to the full U.S. Prescribing Information and Medication Guide for ULTOMIRIS and SOLIRIS available via the links below, including the BOXED WARNING regarding serious and life-threatening meningococcal infections for both medicines.

[ULTOMIRIS Full Prescribing Information and Medication Guide](#)

[SOLIRIS Full Prescribing Information and Medication Guide](#)

#### **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 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](http://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: future plans for a clinical trial of ULTOMIRIS for approximately 270 adults with COVID-19 who are hospitalized with severe pneumonia or acute respiratory distress syndrome; the timing of the commencement, conclusion and reporting of results of such clinical trial; we are attempting to rapidly evaluate the potential of C5 inhibition in treating patients with severe COVID-19; Alexion will maintain and commits to continue to supply its medicines to current and future patients for approved indications; complement inhibition may improve coronaviral-mediated lung injury; Alexion believes ULTOMIRIS represents the future of C5 inhibition, and it may reduce the burden on hospital systems with less frequent dosing and can be manufactured at a higher capacity, providing the opportunity to better meet future supply demands; Alexion will strive to maintain sufficient inventory levels to continue serving current and new patients receiving our medicines for approved indications as well as those participating in ongoing clinical trials; should the role of C5 in treating severe respiratory complications of COVID-19 be demonstrated in a controlled clinical trial, there is the potential for significantly increased demand for our C5 inhibitors; Alexion is working to prepare for potential increased demand and other potential scenarios that may arise so that we are ready to support access; Alexion will continue to monitor and manage the production of ULTOMIRIS, appropriately taking into consideration the needs of current and new patients, required inventory levels, anticipated potential supply needs related to COVID-19 and the time-intensive and complex manufacturing process to produce monoclonal antibodies while maintaining the company's rigorous quality standards; the Company is prepared to support the appropriate government agencies in their efforts to address the public health crisis caused by the COVID-19 pandemic, and to leverage our expertise in complement biology to the extent it may help address this novel threat; ULTOMIRIS may have a positive impact in mitigating the certain harm and injury caused by COVID-19; and the Company believes that the outcomes reported to-date warrant conducting a controlled clinical program to explore the impact of C5 inhibition with ULTOMIRIS and establish clinical evidence supporting the role of terminal complement in coronaviral pneumonia. 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: SOLIRIS and/or ULTOMIRIS may not have any beneficial impact on any patients with COVID-19; ULTOMIRIS may not be a safe and/or effective treatment for any patients with COVID-19; the risks of ULTOMIRIS as a treatment for patients with COVID-19 may exceed any benefits of the therapy; the FDA (and any other regulatory agency) may not approve ULTOMIRIS as a treatment for COVID-19 or a subset of patients with COVID-19; any potential regulatory approval of ULTOMIRIS as a treatment for COVID-19, even if obtained, may be delayed; there may be competing therapies for COVID-19 and ULTOMIRIS may not gain market

acceptance; the anticipated benefits of ULTOMIRIS for any COVID-19 patients may not be realized (and the results of the clinical trials may not be indicative of the results once approved for use in a broader population); results of clinical trials may not be sufficient to satisfy the FDA or any other regulatory authority in order to approve ULTOMIRIS as a treatment for COVID-19 patients (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 (including due to capacity constraints at trial sites due to COVID-19); 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; inability to meet expected demand for our products due to manufacturing issues (at Alexion or at third parties), supply chain issues or otherwise; our manufacturing and third-party manufacturing may not be sufficient to meet product demand for ULTOMIRIS (including due to manufacturing employee exposure to COVID-19); we may not be able to maintain sufficient inventory of product; we may be unable to deliver our products (due to transportation interruption as a result of COVID-19); 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 C5 inhibitor products; 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 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 FDA and other regulatory agencies regarding products and product candidates; 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; 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 (SEC) and U.S. Department of Justice; the risk that estimates regarding the number of patients with PNH, aHUS, gMG, NMOSD, HPP, COVID-19 and LAL-D and other indications we are pursuing are inaccurate; the risks of changing foreign exchange rates; 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 Annual Report on Form 10-K for the year ended December 31, 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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<sup>i</sup> Gralinski LE, Sheahan TP, Morrison TE, et al. Complement activation contributes to severe acute respiratory syndrome coronavirus pathogenesis. *mBio*. 2018;9(5). doi:10.1128/mBio.01753-18.

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