ULTOMIRIS® (ravulizumab) Receives Marketing Authorization from Japan's Ministry of Health, Labour and Welfare (MHLW) for the Treatment of Adults with Paroxysmal Nocturnal Hemoglobinuria (PNH)

June 18, 2019

- Physicians in Japan will soon be able to prescribe a treatment for PNH that requires fewer infusions, reducing the treatment burden for patients -

- ULTOMIRIS has the potential to become the new standard of care for both complement inhibitor-naïve patients and patients switching from SOLIRIS® (eculizumab) -

BOSTON--(BUSINESS WIRE)--Jun. 18, 2019-- **Alexion Pharmaceuticals, Inc.** (NASDAQ:ALXN) today announced that Japan's Ministry of Health, Labour and Welfare (MHLW) has approved ULTOMIRIS® (ravulizumab), the first and only long-acting C5 complement inhibitor administered every eight weeks, for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

PNH is an ultra-rare and severe disease that, when left untreated, may cause a wide range of debilitating symptoms and complications, including thrombosis. Thrombosis occurs when a blood clot presents inside a blood vessel, and slows or blocks the flow of blood through the circulatory system. Serious cases of thrombosis can occur throughout the body and result in organ damage, stroke, heart attack, and potentially premature death.[1–8]

"As a physician, I am pleased to have a new medication for patients in Japan facing the burden of living with PNH—both for people naive to anti-complement therapy and those that are already on SOLIRIS seeking to make a change without interruption," said Jun-ichi Nishimura, M.D., Ph.D. Assistant Professor, Department of Hematology and Oncology, Osaka University Graduate School of Medicine, Japan. "When PNH is not treated, the consequences can be serious."

PNH can strike men and women of all races, backgrounds and ages without warning, with an average age of onset in the early 30s.[1,9] PNH often goes unrecognized, with delays in diagnosis ranging from one to more than five years.[10]

The Ministry's approval is based on comprehensive results from two Phase 3 studies, which were published in *Blood*.[11,12] In these studies, which included 441 patients who had either never been treated with a complement inhibitor before, or who had been stable on SOLIRIS, the efficacy of ULTOMIRIS administered every eight weeks was non-inferior to the efficacy of SOLIRIS administered every two weeks on all 11 endpoints. The safety profile of ULTOMIRIS was similar to that of SOLIRIS. Additional data showed that ULTOMIRIS provided immediate and complete C5 inhibition that was sustained for eight weeks[13] and that ULTOMIRIS eliminated breakthrough hemolysis associated with incomplete C5 inhibition.[14] The entire clinical development program for ULTOMIRIS to date represents more than 800 patient years of experience.

"Immediate and complete C5 inhibition with ULTOMIRIS can provide meaningful benefits for patients and their families," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "Based on the totality of our compelling data from the largest Phase 3 program ever conducted in PNH, we believe ULTOMIRIS has the potential to become the new standard of care for patients with PNH in Japan. We would like to express our deep gratitude to the patients and investigators in Japan who supported this study with their participation."

About Paroxysmal Nocturnal Hemoglobinuria (PNH)
Paroxysmal nocturnal hemoglobinuria (PNH) is a chronic, progressive, debilitating and life-threatening ultra-rare blood disorder characterized by hemolysis (destruction of red blood cells) that is mediated by an uncontrolled activation of the complement system, a component of the body's immune system.[1,2,15] PNH can strike men and women of all races, backgrounds and ages without warning, with an average age of onset in the early 30s.[1,9] PNH often goes unrecognized, with delays in diagnosis ranging from one to more than five years.[10] Patients with PNH may experience a wide range of signs and symptoms, such as fatigue, difficulty swallowing, shortness of breath, abdominal pain, erectile dysfunction, dark-colored urine and anemia.[3–5,7,8,11,15] The most devastating consequence of chronic hemolysis is thrombosis, which can occur in blood vessels throughout the body, damage vital organs and cause premature death.[16] The first thrombotic event can be fatal.[1,9,17] Despite historical supportive care, including transfusion and anticoagulation management, 20 to 35 percent of patients with PNH die within five to 10 years of diagnosis.[18,19] Patients with certain types of hemolytic anemia, bone marrow disorders and unexplained venous or arterial thrombosis are at increased risk of PNH.[15,20–24]

About ULTOMIRIS®
ULTOMIRIS (ravulizumab), the first and only long-acting C5 inhibitor administered every eight weeks, is approved in the U.S. and Japan as a treatment for adults with paroxysmal nocturnal hemoglobinuria (PNH). ULTOMIRIS works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system. The terminal complement cascade, when activated in an uncontrolled manner, plays a role in severe ultra-rare disorders like PNH, atypical hemolytic uremic syndrome (aHUS), anti-acetylcholine receptor (AchR) antibody-positive myasthenia gravis (MG) and anti-aquaporin-4 (AQP4) auto-antibody-positive neuromyelitis optica spectrum disorder (NMOSD). In Phase 3 clinical studies in complement inhibitor-naïve patients with PNH[11] and patients with PNH who had been stable on SOLIRIS® (eculizumab),[12] intravenous treatment with ULTOMIRIS every eight weeks demonstrated non-inferiority to intravenous treatment with SOLIRIS every two weeks on all 11 endpoints.

The Phase 3 study of ULTOMIRIS, administered intravenously every eight weeks in adult patients with aHUS, met its primary objective. Alexion has submitted a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) for approval of ULTOMIRIS as a treatment for patients with aHUS and plans to submit similar applications in the EU and Japan later in 2019. ULTOMIRIS is also currently being evaluated in a Phase 3 clinical study in children and adolescents with aHUS, administered intravenously every eight weeks. Alexion has initiated a Phase 3 study of ULTOMIRIS, intravenously administered every eight weeks, as a potential treatment for patients with generalized MG (gMG), and is

planning to initiate a Phase 3 in patients with NMOSD. In addition, Alexion has initiated Phase 3 studies of ULTOMIRIS delivered subcutaneously once per week as a potential treatment for patients with PNH, aHUS and gMG.

ULTOMIRIS has received Orphan Drug Designation (ODD) for the treatment of patients with PNH in the U.S. and Japan and for the subcutaneous treatment of patients with aHUS in the U.S.

U.S. Indication of ULTOMIRIS® (ravulizumab-cwvz)
ULTOMIRIS is a prescription medicine called a monoclonal antibody. ULTOMIRIS is used to treat adults with a disease called paroxysmal nocturnal hemoglobinuria (PNH). It is not known if ULTOMIRIS is safe and effective in children.

U.S. Important Safety Information for ULTOMIRIS® (ravulizumab-cwvz)
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. 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 with a stiff neck or stiff back, fever and a rash, muscle aches with flu-like symptoms, headache and fever, fever, confusion, and eyes sensitive to light.

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 healthcare provider. Call the healthcare provider right away if one has any new signs or symptoms of infection.

Before one receives ULTOMIRIS, tell the doctor about all of the medical conditions, including if one: has an infection or fever, is pregnant or plans to become pregnant, and is breastfeeding or plans 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 breast feed 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 medications 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 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 number of the red blood cell count, tiredness, blood in the urine, stomach-area (abdomen) pain, blood clots, shortness of breath, trouble swallowing, and erectile dysfunction (ED) in males.

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, or feeling faint. 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 are upper respiratory infection and headache.

For more information, please see the full U.S. Prescribing Information and Medication Guide for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections/sepsis, also available at: www.ultomiris.com.

U.S. Important Safety Information for SOLIRIS® (eculizumab)
SOLIRIS is a medicine that affects the immune system. SOLIRIS can lower the ability of the immune system to fight infections. SOLIRIS 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 SOLIRIS if one has not already had this vaccine. If one's doctor decided that urgent treatment with SOLIRIS is needed, meningococcal vaccination should be administered as soon as possible. If one has not been vaccinated and SOLIRIS 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 SOLIRIS. 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.

SOLIRIS is only available through a program called the SOLIRIS REMS.

SOLIRIS may also increase the risk of other types of serious infections. If one's child is treated with SOLIRIS, make sure that the child receives vaccinations against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). Certain people may be at risk of serious infections with gonorrhea. Talk to the doctor about whether one is at risk for gonorrhea infection, about gonorrhea prevention, and regular testing. Certain fungal infections (Aspergillus) may also happen if one takes SOLIRIS and has a weak immune system or a low white blood cell count.

Before one receives SOLIRIS, tell the doctor about all of the medical conditions, including if one: has an infection or fever, is pregnant or plans to become pregnant, and is breastfeeding or plans to breastfeed. It is not known if SOLIRIS will harm an unborn baby. It is not known if SOLIRIS passes into the breast milk.

Tell the doctor about all the medicines one takes, including prescription and over-the-counter medicines, vitamins, and herbal supplements. SOLIRIS

and other medicines can affect each other causing side effects.

It is important that one: has all recommended vaccinations before starting SOLIRIS, receives 2 weeks of antibiotics if one immediately starts SOLIRIS, and stays up-to-date with all recommended vaccinations during treatment with SOLIRIS. Know the medications 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, the doctor will need to monitor closely for at least 8 weeks after stopping SOLIRIS. Stopping treatment with SOLIRIS 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 number of the red blood cell count, drop in the platelet counts, confusion, kidney problems, blood clots, difficulty breathing, and chest pain.

If one has aHUS, the doctor will need to monitor closely for at least 12 weeks after stopping SOLIRIS 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, swellings in arms or legs and a drop in platelet count.

SOLIRIS can cause serious side effects including serious allergic reactions. Serious allergic reactions can happen during one's SOLIRIS infusion. Tell the doctor or nurse right away if one gets 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 one 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.

Please see the accompanying full U.S. Prescribing Information and Medication Guide for SOLIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections, also available at: www.soliris.net.

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 therapies. 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) as well as the first and only approved complement inhibitor to treat atypical hemolytic uremic syndrome (aHUS) and anti-acetylcholine receptor (AchR) antibody-positive generalized myasthenia gravis (gMG), and is also developing it for patients with 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 second complement inhibitor, a copper-binding agent for Wilson disease and an anti-neonatal Fc receptor (FcRn) antibody for rare Immunoglobulin G (IgG)-mediated diseases as well as several early-stage therapies, including one for light chain (AL) amyloidosis and a second anti-FcRn therapy. 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, and metabolic disorders. Alexion has been named to the Forbes list of the World's Most Innovative Companies seven years in a row and is headquartered in Boston, Massachusetts' Innovation District. The company also 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 Statements
This presentation contains forward-looking statements, including statements related to: the belief that ULTOMIRIS has the potential to become the new standard of care for patients with PNH (including those in PNH patients in Japan); the Company's plans to make future regulatory filings for approval of certain products and product candidates and the timing of such filings, including applications for approval of ULTOMIRIS in the EU and Japan later in 2019 for patients with aHUS; ULTOMIRIS intravenously administered every eight weeks is a potential treatment for patients with gMG; the Company's plans for future clinical trials and studies (including plans to initiate a Phase 3 trial in patients with NMOSD), the timing for the commencement of future clinical trials and the expected timing of the receipt of results of certain clinical trials and studies; ULTOMIRIS subcutaneously administered once per week is a potential treatment for patients with PNH, aHUS and gMG; and the potential benefits of current products and products under development and in clinical trials (including ULTOMIRIS as a treatment for patients with PNH). Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ materially from those forward-looking statements, including for example: any potential post-approval restrictions that the MHLW or any other regulatory agency may impose on Ultomiris; Ultomiris and other products and product candidates do not gain regulatory approval from the MHLW, FDA, EMA or other regulatory authorities; 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; our products, including ULTOMIRIS do not gain acceptance among patients and/or physicians and do not become the standard of care for certain indications; 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); our inability to facilitate the timely conversion of PNH patients (and any future indications) from Soliris to Ultomiris; payer, physician and patient acceptance of Ultomiris as an alternative to Soliris; appropriate pricing for Ultomiris; future competition from biosimilars and novel products (and such future competition causes ULTOMIRIS not to be the standard of care for certain indications); 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, increased 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 MHLW, FDA and other regulatory agencies regarding products and product candidates; results in early stage clinical trials may not be indicative of full results or results from later stage or larger clinical trials (or in broader patient populations) and do not ensure regulatory approval; 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 halt trials, discontinue sales of our products, delay or prevent us from making regulatory approval filings or result in denial of approval of our product candidates; 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 following commercialization); future product improvements may not be realized due to expense or feasibility or other factors; 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; 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; 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, HPP 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 Quarterly Report on Form 10-Q for the quarter ended March 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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