ULTOMIRIS® (ravulizumab) Receives Approval in Japan for Atypical Hemolytic Uremic Syndrome (aHUS) in Adults and Children

September 25, 2020

– ULTOMIRIS is the first and only long-acting C5 inhibitor for aHUS, reducing the treatment burden for adults and children with administration every other month –

– ULTOMIRIS has the potential to become the new standard of care in Japan for the treatment of aHUS, an ultra-rare disease which may progressively damage the kidney and other organs –

BOSTON--(BUSINESS WIRE)--Sep. 25, 2020-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced that Japan's Ministry of Health, Labour and Welfare (MHLW) approved ULTOMIRIS® (ravulizumab) for adults and children living with atypical hemolytic uremic syndrome (aHUS). ULTOMIRIS is the first and only long-acting C5 inhibitor for aHUS and is administered every other month for adults and children (20 kg or more) and monthly for children (<20 kg). Atypical HUS is an ultra-rare disease that can cause progressive injury to vital organs, primarily the kidneys, via damage to the walls of blood vessels and blood clots.

"The goal of aHUS treatment is to prevent the body from attacking its own immune system through the inhibition of uncontrolled C5 complement activation," said Prof. Shoichi Maruyama, Director, Department of Nephrology, Nagoya University Hospital. "Importantly, ULTOMIRIS demonstrated good control, while also offering more time between infusions, which provides a relevant difference to patients and providers."

Atypical HUS affects both adults and children and many patients present in critical condition in the hospital setting, often requiring supportive care, including dialysis, in an intensive care unit. The prognosis of aHUS can be poor in many cases, with 56 percent of adults and 29 percent of children developing end-stage renal disease or dying within a year of diagnosis with supportive care alone, so a timely and accurate diagnosis in addition to treatment, is critical to improving patient outcomes.

"Today's approval marks another important step in our efforts to continue innovating for patients and improving their treatment experience," said John Orloff, M.D., Executive Vice President and Head of Research & Development at Alexion. "ULTOMIRIS' extended dosing interval offers patients more flexibility and time to focus on living their lives beyond their disease while also reducing the burden on healthcare systems, hospitals and providers, which are all under a tremendous amount of stress in the current environment."

The approval is based on data from two ongoing, global, single-arm open-label studies of ULTOMIRIS – one in adults and one in children, referred to as pediatrics in the study. A total of 18 out of 21 complement inhibitor treatment-naïve children and 56 out of 58 complement inhibitor treatment-naïve adults were enrolled and included in the interim analysis. Efficacy evaluation of Complete TMA Response was defined by normalization of hematologic parameters (platelet count and LDH) and improved kidney function (as measured by ≥25 percent improvement in serum creatinine from baseline). In the initial 26-week treatment periods, 54 percent of adults and 77.8 percent (interim data) of children demonstrated Complete TMA Response. Treatment with ULTOMIRIS resulted in normalization of platelet count in 84 percent of adults and 94 percent of children, normalization of LDH (marker of hemolysis) in 77 percent of adults and 90 percent of children, and improved kidney function in 59 percent of adults and 83 percent (interim data) of children (for patients on dialysis at enrollment, baseline was established after they had come off dialysis). In the 52-week follow-up period, 4 additional adult patients and 3 pediatric patients had a Complete TMA Response that was confirmed after the 26-week Initial Evaluation Period resulting in an overall Complete TMA Response of 61 percent in adults and 94 percent in children (interim data). A second cohort of 10 pediatric patients who were SOLIRIS-experienced were included in the pediatric study, demonstrating that switching to ULTOMIRIS maintained disease control as evidenced by stable hematologic and renal parameters, with no apparent impact on safety.

The most frequently observed adverse reactions reported in these studies were upper respiratory tract infection, diarrhea, nausea, fatigue, headache, nasopharyngitis, and pyrexia. Serious meningococcal infections have occurred in patients treated with ULTOMIRIS, however in aHUS studies, no meningococcal infections occurred in the 89 patients receiving treatment with ULTOMIRIS. To minimize the risk for patients, specific risk-mitigation plans, including a Risk Management Plan, have been established for ULTOMIRIS.

ULTOMIRIS will be available at approval for the treatment of aHUS.

About Atypical Hemolytic Uremic Syndrome (aHUS)

aHUS is an ultra-rare disease that can cause progressive injury to vital organs, primarily the kidneys, via damage to the walls of blood vessels and blood clots. aHUS occurs when the complement system—a part of the body's immune system—over-responds, leading the body to attack its own healthy cells. aHUS can cause sudden organ failure or a slow loss of function over time—potentially resulting in the need for a transplant, and in some cases, death. aHUS affects both adults and children, and many patients present in critical condition, often requiring supportive care, including dialysis, in an intensive care unit. The prognosis of aHUS can be poor in many cases, so a timely and accurate diagnosis—in addition to treatment—is critical to improving patient outcomes. Available tests can help distinguish aHUS from other hemolytic diseases with similar symptoms.

About ULTOMIRIS®

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 every four weeks for pediatric patients less than 20 kg, following a loading dose. ULTOMIRIS is approved in Japan as a treatment for adults with paroxysmal nocturnal hemoglobinuria (PNH). To learn more about the regulatory status of ULTOMIRIS in the countries that we serve, please visit www.alexion.com.

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 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.

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For patient or advocacy inquiries please contact *patientadvocacy@alexion.com*.

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: the impact to Alexion of ULTOMIRIS approval in Japan for adults and children living with atypical hemolytic uremic syndrome (aHUS); that ULTOMIRIS provides effective disease control and together with its dosing, makes a difference to patients; that ULTOMIRIS has the potential to become the new standard of care in Japan for the treatment of aHUS; timely and accurate diagnosis of aHUS patients– in addition to treatment – is critical to improving patient outcomes; the approval of ULTOMIRIS in Japan for aHUS marks another important step in our efforts to continue innovating for patients and improving their treatment experience; and ULTOMIRIS' extended eight-week dosing interval offers patients more flexibility and time to focus on living their lives beyond their disease while also reducing the burden on healthcare systems, hospitals and providers. 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: the anticipated benefits of ULTOMIRIS for aHUS patients may not be realized (and the results of the clinical trials may not be indicative of the results in Japan); results of clinical trials may not be sufficient to satisfy any other regulatory authority in order to approve ULTOMIRIS as a treatment for aHUS (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; 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; 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 principal product (Soliris); 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 failure of product candidates to obtain regulatory approval; 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 regulatory agencies regarding products and product candidates; uncertainty of long-term success in developing, licensing or acquiring other product candidates or additional indications for existing products; inability to complete acquisitions or grow the product pipeline through acquisitions (including due to failure to obtain antitrust approvals); 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; 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 the coronavirus; uncertainties surrounding legal proceedings, company investigations and government investigations; the risk that estimates regarding the number of patients with PNH, aHUS, gMG, NMOSD, HPP and LAL-D and other indications we are pursuing are inaccurate; the risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructuring; risks related to the acquisition of Achillion, Portola and other companies and co-development efforts; 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 period ended June 30, 2020 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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Alexion:
Media
Megan Goulart, 857-338-8634
Executive Director, Corporate Communications

Investors

Chris Stevo, 857-338-9309
Head of Investor Relations

Source: Alexion Pharmaceuticals, Inc.