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## **Alexion's Soliris® (eculizumab) Receives Marketing Approval in Japan for All Patients with aHUS**

*First and Only Approved Treatment in Japan for Patients Suffering from aHUS, a Chronic and Life-Threatening Ultra-Rare Disease*

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq:ALXN), today announced that the Ministry of Health, Labour and Welfare (MHLW) in Japan has approved the use of Soliris® (eculizumab) for the treatment of pediatric and adult patients with atypical hemolytic uremic syndrome (aHUS), a life-threatening ultra-rare disorder. Soliris is already approved in Japan for paroxysmal nocturnal hemoglobinuria (PNH), another severe and ultra-rare disease. Alexion expects that initial patients with aHUS in Japan will commence treatment with Soliris during the fourth quarter of this year.

aHUS is a life-threatening and ultra-rare chronic genetic disease that can progressively damage vital organs, leading to stroke, heart attack, kidney failure, and death.<sup>1</sup> The morbidities and premature mortality in aHUS is caused by chronic uncontrolled activation of the complement system, resulting in thrombotic microangiopathy (TMA, the formation of blood clots in small blood vessels throughout the body).<sup>2,3</sup> Soliris, a first-in-class terminal complement inhibitor, specifically targets uncontrolled complement activation, and is approved for the suppression of TMA in patients with aHUS.

"Soliris has been proven to have a life-transforming impact on patients suffering from aHUS and represents a significant step forward in the treatment of this devastating disease," said Prof. Motoshi Hattori, Professor and Director of the Department of Pediatric Nephrology, Tokyo Women's Medical University of Tokyo Woman's UHP. "Results from clinical studies show that chronic Soliris treatment inhibits complement-mediated TMA which is responsible for thrombosis, vital organ failure, and other life-threatening manifestations of aHUS."

"The approval of Soliris for the treatment of aHUS by the Japanese government brings life-transforming hope to patients suffering from this devastating disease," said David Hallal, Executive Vice President and Chief Commercial Officer of Alexion. "We will initiate our disease awareness and education programs as we work closely with the healthcare community to support rapid and accurate diagnosis of aHUS as well as better informed treatment decisions."

Soliris is also approved by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) and other regulatory authorities for the treatment of patients with aHUS to inhibit complement-mediated TMA. In addition, Soliris is approved in more than 40 countries, including Japan, for the treatment of patients with PNH, a debilitating, ultra-rare and life-threatening blood disorder.

### **Clinical Data**

Alexion's supplemental new drug application (sNDA) for Soliris in Japan included clinical data from two prospective, controlled, open-label studies in adolescent and adult patients with aHUS, and a third retrospective study in pediatric patients with aHUS, which together included a broad range of aHUS patients in North America and Europe. In these studies, all patients treated with Soliris demonstrated rapid and sustained reduction in terminal complement activity, and chronic administration of Soliris resulted in rapid and sustained reduction in complement-mediated TMA. Soliris was well tolerated in these clinical studies. The most frequently reported adverse events were hypertension, upper respiratory tract infection, and diarrhea. In addition, the sNDA in Japan included data from a retrospective study and from an ongoing prospective study of both pediatric and adult aHUS patients in Japan. Results from these studies demonstrated that the safety and efficacy of Soliris in these Japanese patients with aHUS were consistent with those noted in the clinical studies of Soliris in aHUS patients in North America and Europe.

### **About aHUS**

aHUS is a chronic, ultra-rare, and life-threatening disease in which a genetic deficiency in one or more complement regulatory genes causes chronic uncontrolled complement activation, resulting in complement-mediated thrombotic microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body.<sup>4,5</sup> Permanent, uncontrolled complement activation in aHUS causes a life-long risk for TMA, which leads to sudden, catastrophic, and life-threatening damage to the kidney, brain, heart, and other vital organs, and premature death.<sup>4,6</sup> Sixty-five percent of all patients with aHUS die, require kidney dialysis, or have permanent kidney damage within the first year after diagnosis despite plasma exchange or plasma

infusion (PE/PI).<sup>3,7</sup> The majority of patients with aHUS who receive a kidney transplant commonly experience subsequent systemic TMA, resulting in a 90% transplant failure rate in these TMA patients.<sup>8</sup>

aHUS affects both children and adults. Complement-mediated TMA also causes reduction in platelet count (thrombocytopenia) and red blood cell destruction (hemolysis). While mutations have been identified in at least ten different complement regulatory genes, mutations are not identified in 30-50% of patients with a confirmed diagnosis of aHUS.<sup>2</sup>

### **About Soliris**

Soliris is a first-in-class terminal complement inhibitor developed from the laboratory through regulatory approval and commercialization by Alexion. Soliris is also approved in the US, European Union, Japan and other countries as the first and only treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH), a debilitating, ultra-rare and life-threatening blood disorder, characterized by complement-mediated hemolysis (destruction of red blood cells).

Soliris is also approved in the US, the European Union, Japan and other territories as the first and only treatment for patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy, a debilitating, ultra-rare and life-threatening genetic disorder characterized by complement-mediated thrombotic microangiopathy (blood clots in small vessels). The effectiveness of Soliris in aHUS is based on the effects on thrombotic microangiopathy (TMA) and renal function. Prospective clinical trials in additional patients are ongoing to confirm the benefit of Soliris in patients with aHUS. Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Alexion's breakthrough approach in complement inhibition has received the pharmaceutical industry's highest honors: the 2008 Prix Galien USA Award for Best Biotechnology Product with broad implications for future biomedical research and the 2009 Prix Galien France Award in the category of Drugs for Rare Diseases.

### **Important Safety Information**

The US product label for Soliris includes a boxed warning: "Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies. Immunize patients with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risk of developing a meningococcal infection. (See Serious Meningococcal Infections (5.1) for additional guidance on the management of meningococcal infection.) Monitor patients for early signs of meningococcal infections and evaluate immediately if infection is suspected. Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS, prescribers must enroll in the program. Enrollment in the Soliris REMS program and additional information are available by telephone: 1-888-soliris (1-888-765-4747)."

In patients with PNH, the most frequently reported adverse events observed with Soliris treatment in clinical studies were headache, nasopharyngitis (runny nose), back pain and nausea. Soliris treatment of patients with PNH should not alter anticoagulant management because the effect of withdrawal of anticoagulant therapy during Soliris treatment has not been established. In patients with aHUS, the most frequently reported adverse events observed with Soliris treatment in clinical studies were hypertension, upper respiratory tract infection, diarrhea, headache, anemia, vomiting, nausea, urinary tract infection, and leukopenia. Please see full prescribing information for Soliris, including boxed WARNING regarding risk of serious meningococcal infection.

### **About Alexion**

Alexion Pharmaceuticals, Inc. is a biopharmaceutical company focused on serving patients with severe and ultra-rare disorders through the innovation, development and commercialization of life-transforming therapeutic products. Alexion is the global leader in complement inhibition, and has developed and markets Soliris<sup>®</sup> (eculizumab) as a treatment for patients with PNH and aHUS, two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is currently approved in more than 40 countries for the treatment of PNH, and in the United States, Europe, Japan and other territories for the treatment of aHUS. Alexion is evaluating other potential indications for Soliris and is pursuing development of four other innovative biotechnology product candidates which are being investigated across additional severe and ultra-rare disorders beyond PNH and aHUS. This press release and further information about Alexion Pharmaceuticals, Inc. can be found at [www.alexionpharma.com](http://www.alexionpharma.com).

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### **Safe Harbor Statement**

This news release contains forward-looking statements, including statements related to potential health and medical benefits from Soliris and the timing of regulatory and commercial milestones for Soliris in Japan. Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ from those expected, including for example, decisions of regulatory authorities regarding marketing approval or material limitations on the marketing of Soliris, delays in arranging satisfactory manufacturing capability and establishing commercial infrastructure, delays in developing or adverse changes in commercial relationships, the possibility that results of published reports or clinical trials are not predictive of safety and efficacy results of Soliris in broader patient populations, the risk that clinical trials may not be completed successfully, the possibility that initial results of commercialization are not predictive of future rates of adoption of Soliris, the risk that third parties won't agree to license any necessary intellectual property to Alexion on reasonable terms or at all, the risk that third party payors will not reimburse for the use of Soliris at acceptable rates or at all, and a variety of other risks set forth from time to time in Alexion's filings with the Securities and Exchange Commission, including but not limited to the risks discussed in Alexion's Annual Report on Form 10-Q for the period ended June 30, 2013, and in Alexion's other filings with the Securities and Exchange Commission. Alexion does not intend 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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