



December 8, 2015

## FDA Approves Kanuma™ (sebelipase alfa) for the Treatment of Patients with Lysosomal Acid Lipase Deficiency (LAL-D)

*- Kanuma is the First Approved Treatment in the United States for Patients Suffering from LAL-D, a Life-threatening and Ultra-rare Metabolic Disorder -*

*- Conference Call Scheduled for Tuesday, December 8 at 5:00 p.m. ET -*

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ: ALXN) announced today that the U.S. Food and Drug Administration (FDA) has approved Kanuma™ (sebelipase alfa) for the treatment of patients of all ages with a diagnosis of lysosomal acid lipase deficiency (LAL-D). Kanuma, an innovative enzyme replacement therapy (ERT), is the first therapy approved in the U.S. for the treatment of patients with LAL-D, a genetic and progressive ultra-rare metabolic disease in which patients suffer multi-organ damage and premature death.

This Smart News Release features multimedia. View the full release here:

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"We are pleased with the FDA approval of Kanuma, a transformative treatment for patients with LAL-D, a devastating, ultra-rare disease that causes premature death in infants and multi-organ damage in those who survive," said David Hallal, Chief Executive Officer of Alexion. "Importantly, the label includes a survival benefit in infants and reductions in important markers of liver disease, including ALT and liver fat content, as well as significant improvements in lipid parameters, in children and adults. This approval also strengthens Alexion's global leadership in rare diseases as we broaden our product portfolio to transform the lives of more patients with severe and life-threatening disorders. We look forward to bringing Kanuma to patients with LAL-D and their physicians in the United States."

"I am delighted that patients with LAL-D now have the first approved therapy that treats the underlying cause of the disease," said Barbara K. Burton, M.D., lead clinical trial investigator, Professor of Pediatrics at the Northwestern University Feinberg School of Medicine and Attending Physician at the Ann and Robert H. Lurie Children's Hospital of Chicago. "In the absence of treatment, LAL-D is nearly always fatal in infants and puts pediatric and adult patients at high risk of vital organ damage and premature mortality. In clinical studies, 67% of infants who received enzyme replacement therapy survived beyond 12 months of age, and children and adults had meaningful improvements in multiple disease-related liver and lipid abnormalities."

LAL-D is a genetic, chronic, and progressive metabolic disease associated with significant morbidity and premature mortality. It is an ultra-rare disease, which is defined as a disease that affects fewer than 20 patients per one million of the general population.<sup>1</sup>

Patients with LAL-D can experience a rapid onset of life-threatening disease manifestations, and without treatment, the youngest patients with LAL-D face rapid disease progression that is typically fatal within a matter of months. In addition, similar to other liver diseases, many patients may be asymptomatic until they experience a severe consequence of the disease. LAL-D is caused by genetic mutations that result in a marked decrease or loss in LAL enzyme activity in the lysosomes across multiple body tissues, leading to the chronic build-up of cholesteryl esters and triglycerides in the liver, blood vessel walls, and other organs.<sup>2,3</sup>

"Patients with LAL-D often suffer for years from a delayed diagnosis, only to be further devastated once properly diagnosed because there have been no approved treatments for this disease," said Brett Billmeyer, Board of Directors, LAL Solace.

"Today, we are thrilled to welcome the FDA approval of Kanuma, providing an approved and effective treatment to patients with LAL-D and their families for the first time and, with it, bringing much-needed awareness to this often overlooked and devastating disease."

Alexion will offer support to patients with LAL-D through its OneSource™ program. OneSource provides each patient and family with personalized support from a dedicated Alexion nurse case manager, who can help patients understand their insurance benefits and receive reimbursement assistance. Through OneSource, patients and families can obtain further information regarding third-party foundations and co-pay assistance programs that help patients meet out-of-pocket expenses related to the treatment of LAL-D. For uninsured patients who have no access to insurance, the Alexion Access Foundation, a charitable entity, provides Kanuma free of charge for patients. Patients, caregivers, and healthcare providers in the U.S. can call 1-888-765-4747 to speak with a OneSource nurse case manager.

Alexion is preparing to serve patients in the U.S. with Kanuma and expects that Kanuma will become available commercially during the first week of January 2016. The Company's expanded access program will remain open to enable patients with LAL-D in the U.S. to access Kanuma until commercial product is available.

The FDA approved Kanuma under Priority Review, and had previously granted Breakthrough Therapy Designation for Kanuma for LAL-D presenting in infants. With this approval, the FDA also issued a Rare Pediatric Disease Priority Review Voucher, which confers priority review to a subsequent drug application that would not otherwise qualify for priority review. The rare pediatric disease review voucher program is designed to encourage development of new drugs and biologics for the prevention or treatment of rare pediatric diseases. Kanuma is also approved in the European Union, and a New Drug Application for Kanuma has been submitted to Japan's Ministry of Health, Labour and Welfare.

## Clinical Data<sup>4</sup>

The approval of Kanuma in the U.S. was based on data from two clinical studies and a supporting open-label extension study comprising infant, pediatric, and adult patients with LAL-D. Study results showed significant benefit in terms of survival (67%, or 6 out of 9) in patients with the infant form of LAL-D beyond 12 months, compared with 0 out of 21 patients in an untreated historical cohort. In pediatric and adult patients with LAL-D (ages 4 to 58 years), treatment with Kanuma resulted in larger reductions from baseline in ALT values and liver fat content, as measured by MRI, compared to treatment with placebo. Reduced ALT values were generally seen within 2 weeks. In addition, treated patients had significant improvements in lipid parameters, including LDL-C, HDL-C, non-HDL-C, and triglycerides, compared to placebo. The significance of these findings as they relate to cardiovascular morbidity and mortality or progression of liver disease in LAL deficiency has not been established. Continued improvements in ALT, LDL-C and HDL-C were seen in patients treated with Kanuma for up to 36 weeks.

The most commonly reported adverse events observed in clinical trials in infants were diarrhea, vomiting, fever, rhinitis, anemia, cough, nasopharyngitis, and urticaria. The most commonly reported adverse events observed in clinical trials in pediatric and adult patients were headache, fever, oropharyngeal pain, nasopharyngitis, asthenia, constipation, and nausea.

## Conference Call

Alexion will host a conference call/webcast today, Tuesday, December 8, 2015, at 5:00 p.m. ET to discuss the FDA approval. To participate in this call, dial (866) 433-3833 (USA) or (704) 908-0448 (international), confirmation code 93767158, shortly before 5:00 p.m. ET. A replay of the call will be available for a limited period following the call, beginning at 8:00 p.m. ET. The replay number is (855) 859-2056 (USA) or (404) 537-3406 (international), confirmation code 93767158. The audio webcast can be found on the Investor page of Alexion's website at: <http://ir.alexionpharm.com>.

## About Lysosomal Acid Lipase Deficiency (LAL-D)

LAL-D is a genetic, chronic, and progressive ultra-rare metabolic disease associated with significant morbidity and premature mortality. In patients with LAL-D, genetic mutations result in decreased activity of the LAL enzyme. This leads to marked accumulation of cholesteryl esters and triglycerides in vital organs, blood vessels, and other tissues, resulting in progressive and multi-organ damage including fibrosis, cirrhosis, liver failure, accelerated atherosclerosis, cardiovascular disease, and other devastating consequences.<sup>2,3</sup>

LAL-D affects patients of all ages with clinical manifestations from infancy through adulthood and may have sudden and unpredictable clinical complications. Infants experience profound growth failure, liver fibrosis, and cirrhosis, with a median age of death at 3.7 months.<sup>5</sup> In an observational study, approximately 50% of children and adults with LAL-D progressed to fibrosis, cirrhosis, or liver transplant in 3 years.<sup>6</sup> The median age of onset of LAL-D is 5.8 years, and the disease can be diagnosed with a simple blood test.<sup>7,8</sup>

## About Kanuma™ (sebelipase alfa)

Kanuma™ (sebelipase alfa) is an innovative enzyme replacement therapy that addresses the underlying cause of lysosomal acid lipase deficiency (LAL-D) by reducing substrate accumulation in the lysosomes of cells throughout the body. In clinical studies, treatment with Kanuma improved survival in infants with LAL-D and led to significant reductions in ALT and liver fat content, as well as significant improvements in lipid parameters, in children and adults with LAL-D.

Kanuma is approved in the United States and European Union. A New Drug Application for Kanuma has been submitted to Japan's Ministry of Health, Labour and Welfare.

## **IMPORTANT SAFETY INFORMATION:**

### **WARNINGS AND PRECAUTIONS**

Hypersensitivity reactions, including anaphylaxis, have been reported in KANUMA-treated patients. In clinical trials, 3 of 106 (3%) patients treated with KANUMA experienced signs and symptoms consistent with anaphylaxis. These patients experienced reactions during infusion with signs and symptoms including chest discomfort, conjunctival injection, dyspnea, generalized and itchy rash, hyperemia, swelling of eyelids, rhinorrhea, severe respiratory distress, tachycardia, tachypnea, and urticaria. Anaphylaxis has occurred as early as the sixth infusion and as late as 1 year after treatment initiation.

In clinical trials, 21 of 106 (20%) KANUMA-treated patients, including 9 of 14 (64%) infants and 12 of 92 (13%) pediatric patients, 4 years and older, and adults experienced signs and symptoms either consistent with or that may be related to a hypersensitivity reaction. Signs and symptoms of hypersensitivity reactions, occurring in two or more patients, included abdominal pain, agitation, fever, chills, diarrhea, eczema, edema, hypertension, irritability, laryngeal edema, nausea, pallor, pruritus, rash, and vomiting. The majority of reactions occurred during or within 4 hours of the completion of the infusion. Patients were not routinely pre-medicated prior to infusion of KANUMA in these clinical trials.

Due to the potential for anaphylaxis, appropriate medical support should be readily available when KANUMA is administered.

Hypersensitivity to Eggs or Egg Products: Consider the risks and benefits of treatment in patients with known systemic hypersensitivity reactions to eggs or egg products.

### **ADVERSE REACTIONS**

The most common adverse reactions are: In patients with Rapidly Progressive Disease Presenting within the First 6 Months of Life ( $\geq 30\%$ ): diarrhea, vomiting, fever, rhinitis, anemia, cough, nasopharyngitis, and urticaria. In pediatric and adult patients ( $\geq 8\%$ ): headache, fever, oropharyngeal pain, nasopharyngitis, asthenia, constipation, and nausea.

Please [click here](#) for the full Prescribing Information.

### **About Alexion**

Alexion is a global biopharmaceutical company focused on developing and delivering life-transforming therapies for patients with devastating and rare disorders. Alexion developed and commercializes Soliris® (eculizumab), the first and only approved complement inhibitor to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), two life-threatening ultra-rare disorders. As the global leader in complement inhibition, Alexion is strengthening and broadening its portfolio of complement inhibitors, including evaluating potential indications for eculizumab in additional severe and ultra-rare disorders. Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, Strensiq™ (asfotase alfa) to treat patients with hypophosphatasia (HPP) and Kanuma™ (sebelipase alfa) to treat patients with lysosomal acid lipase deficiency (LAD). In addition, Alexion is advancing the most robust rare disease pipeline in the biotech industry, with highly innovative product candidates in multiple therapeutic areas. 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 Statements**

*This news release contains forward-looking statements, including statements related to potential medical benefits of Kanuma™ (sebelipase alfa) for lysosomal acid lipase deficiency (LAL-D). 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 Kanuma for LAL-D, delays in arranging satisfactory manufacturing capabilities and establishing commercial infrastructure for Kanuma for LAL-D, the possibility that results of clinical trials are not predictive of safety and efficacy results of Kanuma in broader or different patient populations, the risk that third party payors (including governmental agencies) will not reimburse for the use of Kanuma at acceptable rates or at all, the risk that estimates*

regarding the number of patients with Kanuma and observations regarding the natural history of patients with Kanuma are inaccurate, 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 Quarterly Report on Form 10-Q for the period ended September 30, 2015 and in Alexion's other filings with the SEC. 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.

## References

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3. Reiner Z, et al. Lysosomal acid lipase deficiency - an under-recognized cause of dyslipidemia and liver dysfunction. Atherosclerosis. 2014;235:21-30. doi:10.1016/j.atherosclerosis.2014.04.003.
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