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New Data Presented at WORLDSymposium™ 2016 Show Substantial Survival Benefit Beyond 2 Years of Age in Infants with Lysosomal Acid Lipase Deficiency (LAL-D) Treated with Kanuma™ (sebelipase alfa)

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq:ALXN) announced today that researchers presented new two-year data from an ongoing, open-label Phase 2/3 trial of Kanuma™ (sebelipase alfa) in infants with lysosomal acid lipase deficiency (LAL-D), a genetic and progressive ultra-rare metabolic disease. Data from this study demonstrated a substantial survival benefit (56 percent, or 5 out of 9) to beyond 2 years of age for patients with rapidly progressive LAL-D during infancy who were treated with Kanuma, with the longest-treated patient surviving to over 5 years of age.¹ Patients also had improvements in a number of key parameters, including weight gain, important markers of liver disease, gastrointestinal symptoms, anemia, and hepatosplenomegaly (enlargement of both the liver and spleen), and 4 out of 5 patients demonstrated normal development.¹ These data were reported in an oral presentation at the 12th Annual *WORLDSymposium™* in San Diego. Additionally, researchers reported favorable findings from an analysis of safety data from three ongoing, long-term trials evaluating Kanuma in children and adults with LAL-D.²

"Infants with rapidly progressive LAL-D are missing a vital enzyme and, without treatment, experience multi-organ damage and a high risk of death, typically before their first birthday. The data presented at *WORLDSymposium* demonstrate a meaningful survival benefit to beyond 2 years of age for the most vulnerable patients with LAL-D when treated with Kanuma," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "Moreover, the majority of these young children are developing normally and improving across multiple disease parameters, including important markers of liver disease. Alexion is committed to continuing to serve all patients with this devastating and life-threatening disease."

LAL-D is a genetic, chronic and progressive ultra-rare metabolic disease associated with significant morbidity and premature mortality.³ Ultra-rare diseases are defined as diseases that affect fewer than 20 patients per 1 million of the general population.⁴ 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 vital 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.^{3,5}

In addition to the clinical trial data that were presented, Kanuma will receive the *WORLDSymposium* 2016 New Treatment Award for achieving regulatory approval in both the United States and European Union. The award recognizes important therapeutic achievements in lysosomal disease therapy.

Kanuma is the only approved therapy to address the underlying cause of LAL-D. In addition to Alexion's robust clinical trial program for Kanuma in infants, children, and adults with LAL-D, we have initiated a global registry of LAL-D patients to advance the understanding of this ultra-rare disease.

Improvements in Survival and Key Disease Parameters Beyond 2 Years of Age in Infants Treated with Kanuma¹

In an oral session, data were presented from an ongoing multicenter, open-label, Phase 2/3 study of Kanuma in infant patients with LAL-D who presented with growth failure or other evidence of rapidly progressive disease within the first 6 months of life. At baseline, all 9 patients enrolled in the study had significant liver dysfunction, and 8 had early growth failure.

Researchers reported that of the 9 infants treated with Kanuma, 5 (56 percent) survived beyond 2 years of age (range 2 years and 11 months to 5 years and 2 months). All 5 surviving patients continue to receive Kanuma, with a median time in the trial of 3 years and 2 months. As of the January 2016 data cut-off, the oldest patient had been receiving treatment for 4 years and 10 months. Of the 4 deaths that occurred, all were considered unrelated or likely unrelated to Kanuma and deemed to be related to underlying disease or complications of an abdominal paracentesis. Three of these patients died after receiving ≤4 doses of Kanuma. In a natural history study, without treatment, 0 out of 21 (0 percent) infants with a similar age at disease presentation and clinical characteristics survived beyond 8 months of age.⁶

Patients also demonstrated improvements in key disease parameters with Kanuma treatment, including weight, markers of liver disease, hematological profile, gastrointestinal manifestations, and hepatosplenomegaly. Median weight percentile increased from 3.7 percent at baseline to 31.8 percent at data cut-off. Additionally, 4 out of 5 patients demonstrated normal development, as assessed by their last Denver II developmental screening test, which includes measurements of social contact, fine motor skill, language, and gross motor skill.

"It is extremely gratifying that the survival benefit of Kanuma in infants with LAL-D persisted with continued treatment, allowing more than half of patients to survive beyond 2 years without experiencing the devastating consequences of disease progression," said lead investigator Simon A. Jones, M.D., Central Manchester University Hospitals NHS Foundation Trust and The University of Manchester, Manchester, UK. "We are very pleased that improvements in survival were accompanied by improvements in multiple disease activity parameters, including weight gain, as well as normal development in most patients."

The majority (92 percent) of adverse events were mild to moderate in intensity. Four treatment-related serious AEs occurred in a single patient (pyrexia, pallor, chills, and tachycardia) in association with the same infusion. No patient discontinued the study because of tolerability or infusion-associated reactions.

Favorable Safety Findings from Three Trials of Kanuma in Children and Adults with LAL-D²

In an oral session, data were presented from a long-term safety analysis of 105 children and adults with LAL-D (ranging in age from 3 years to 59 years) from three ongoing clinical trials of Kanuma: a pivotal Phase 3 study (the ARISE study) with a 20-week double-blind, placebo-controlled treatment period followed by open-label treatment with Kanuma; a Phase 2 open-label, single-arm extension study (CL04); and a Phase 2 supporting open-label, single-arm study (CL06). At the time of the data analysis, patients had been treated between 42 and 208 weeks.

Researchers reported that most treatment-emergent adverse events (TEAEs) across the three ongoing studies were mild to moderate in severity and were unrelated to treatment with Kanuma. There were no withdrawals or deaths due to TEAEs. Related serious TEAEs were reported in a total of 3 patients (3 percent), all of which were infusion-associated reactions. A total of 19 patients (18 percent) experienced an infusion-associated reaction. Of 9 patients (9 percent) who had detectable anti-drug antibodies, none experienced a severe or serious adverse event or discontinued treatment due to an adverse event. Researchers concluded that these findings reflect a favorable safety profile for Kanuma in children and adults with LAL-D.

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.³ In patients with LAL-D, genetic mutations result in a marked decrease or loss in activity of the vital 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.^{3,5}

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.⁷ In an observational study, approximately 50 percent of children and adults with LAL-D progressed to fibrosis, cirrhosis, or liver transplant in 3 years.⁸ The median age of onset of LAL-D is 5.8 years, and the disease can be diagnosed with a simple blood test.^{9,10}

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 percent) 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 percent) KANUMA-treated patients, including 9 of 14 (64 percent) infants and 12 of 92 (13 percent) 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 (≥ 30 percent): diarrhea, vomiting, fever, rhinitis, anemia, cough, nasopharyngitis, and urticaria. In Pediatric and Adult Patients (≥ 8 percent): 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 (LAL-D). 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.

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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, risks and uncertainties of drug development, 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 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 Annual Report on Form 10-K for the period ended December 31, 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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