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New Long-Term Data Presented at AASLD Show Reduction in Liver Fibrosis and Cirrhosis in a Cohort of Patients with Lysosomal Acid Lipase Deficiency (LAL-D) Treated with Kanuma® (sebelipase alfa)

--Longer Duration of Kanuma Treatment Associated with Greater Reductions in Fibrosis Stage--

--Additional Long-Term Data Show Rapid and Sustained Reduction in ALT, a Marker of Liver Injury, in 98 Percent of Kanuma-Treated Patients at 76 Weeks--

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) announced today that researchers presented new longer-term data from an ongoing, open-label extension of the pivotal Phase 3 ARISE trial of Kanuma® (sebelipase alfa) in children and adults with lysosomal acid lipase deficiency (LAL-D), a genetic and progressive ultra-rare metabolic disease. Two-thirds of patients (8/12) treated with Kanuma for 52 weeks had a reduction in liver fibrosis stage from baseline, as measured by Ishak score. Moreover, half of patients (6/12) achieved at least a 2-stage reduction, including five patients who had fibrosis at baseline and one who had cirrhosis at baseline. Reduction of liver fibrosis stage was accompanied by sustained improvements in alanine aminotransferase (ALT), LDL cholesterol (LDL-C), and liver fat content through 52 weeks of Kanuma treatment.[1] These data were reported in a poster presentation at The Liver Meeting 2016, the annual meeting of the American Association for the Study of Liver Diseases (AASLD), in Boston.

Researchers at AASLD also presented new long-term data from the ARISE study showing rapid and sustained improvements in important markers of liver injury and lipid abnormalities in children and adults with LAL-D treated with Kanuma. With 76 weeks of Kanuma treatment, nearly all patients (98 percent) had a sustained reduction in ALT levels, with a mean reduction from baseline of 56 percent.[2]

"LAL-D is a devastating and life-threatening disease in which half of children and adults will progress to fibrosis, cirrhosis, or liver transplant within just three years. We are very encouraged that the data presented at AASLD show, for the first time, that Kanuma may have the potential to halt and even reverse the progression of liver damage for patients receiving ongoing treatment," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "Importantly, the greatest impact was observed in those patients who had more significant liver fibrosis at baseline. Findings from this study support the value of early and long-term treatment with Kanuma."

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 typically face premature death within a matter of months. Unfortunately, children and adults with LAL-D are often undiagnosed or misdiagnosed, despite experiencing progressive organ damage that can lead to severe and life-threatening outcomes. 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]

Kanuma is the only approved therapy to address the underlying cause of LAL-D.

Change in Liver Fibrosis in Children and Adults with Lysosomal Acid Lipase Deficiency After 52 Weeks of Sebelipase Alfa (ARISE Trial)[1]

Researchers presented data from the ongoing, open-label period of the Phase 3 ARISE (Acid Lipase Replacement Investigating Safety and Efficacy) trial of Kanuma in children and adults with LAL-D that evaluated the effect of long-term Kanuma treatment on liver fibrosis stage. This poster was selected as a Presidential Poster of Distinction at AASLD. Following the 20-week, double-blind, randomized, placebo-controlled period of the study, 65 patients began the open-label phase and were treated with Kanuma for up to 130 weeks, including 35 patients who were treated with Kanuma during the double-blind period and 30 who were treated with placebo during the double-blind period. Paired liver biopsies were taken in 20 patients (ages 5 to 59 years) at baseline and study Week 52, including 12 patients who initially received Kanuma in the double-blind period and 8 patients who initially received placebo in the double-blind period. The 7-point Ishak staging system was used to assess fibrosis and cirrhosis.

Of the 12 patients who were biopsied at baseline and 52 weeks of Kanuma treatment, six achieved a ≥2-stage reduction in liver fibrosis from baseline, and two achieved a 1-stage reduction. Three patients showed no change in fibrosis stage and one patient had an increase. Of the six patients who had a 2-stage reduction from baseline to week 52, one had cirrhosis and five had stage 3 fibrosis at baseline. In addition to achieving a 2-stage reduction in liver fibrosis, this group of patients demonstrated mean reductions of 61 percent in ALT, 40 percent in LDL-C, and 32 percent in liver fat content after 52 weeks of treatment. Among the 8 patients who were biopsied at baseline and at study week 52 (reflecting 30 weeks of Kanuma treatment), four had a 1-stage reduction in fibrosis, three had no change, and one had an increase.

Additionally, among patients with paired biopsy data at baseline and week 20, a significantly higher proportion of patients in the Kanuma arm had improvement or no change from baseline in hepatic steatosis compared with patients in the placebo arm (94 percent vs. 50 percent; p = 0.0184). Among the 12-patient biopsy cohort that received Kanuma for 52 weeks, median percentage of steatosis decreased by 37 percent from baseline.

"This is the first study to provide evidence of change in Ishak fibrosis score in children and adults with LAL-D treated with Kanuma," said clinical trial investigator Zachary Goodman, M.D., Director of Hepatic Pathology Consultation and Research at Inova Fairfax Hospital, Falls Church, Virginia. "In this cohort of patients, study results showed that longer Kanuma treatment led to greater reductions in fibrosis, with the largest decreases seen after 52 weeks of treatment. The results are extremely encouraging and support the clinical benefits of early and long-term Kanuma treatment in patients with LAL-D."

Most adverse events during the open-label extension period were mild to moderate in intensity. The most common treatment-emergent adverse events were nasopharyngitis, headache, pyrexia, and cough. No patient discontinued the open-label study because of adverse events. Thirteen patients (20 percent) experienced an infusion-associated reaction during the open-label period. One patient had a serious reaction that was considered treatment-related; the patient stopped taking Kanuma but later resumed therapy.

Long-Term Benefit of Sebelipase Alfa over 76 Weeks in Children and Adults with Lysosomal Acid Lipase Deficiency (ARISE Trial)[2]

Researchers at AASLD also presented new 76-week results from the open-label extension of the ARISE trial in patients with LAL-D. Fifty-two week findings were previously reported at the 5th World Congress of Pediatric Gastroenterology, Hepatology and Nutrition (WCPGHAN) in October 2016, demonstrating that nearly all patients (97 percent) who were treated with Kanuma for 52 weeks had a rapid and sustained reduction in ALT, with 47 percent achieving ALT normalization.

New data presented at AASLD showed that after 76 weeks of Kanuma treatment, 98 percent (60/61) of patients had a sustained reduction in ALT from baseline, 51 percent (31/61) achieved ALT normalization, and 65 percent (37/57) achieved aspartate aminotransferase (AST) normalization. Marked and sustained improvements in ALT and AST occurred when patients who had initially received placebo during the double-blind period switched to Kanuma, mirroring those improvements observed in patients receiving Kanuma from the start of the double-blind period. Patients also had improvements in lipid abnormalities, including decreases in mean LDL-C, non-HDL cholesterol, and triglycerides, and increases in mean HDL cholesterol.

"The 76-week ARISE data presented at AASLD continue to reinforce the rapid and sustained improvements in dyslipidemia and markers of liver injury associated with Kanuma," said study investigator Katryn Furuya, M.D., Associate Professor of Pediatrics, Division of Pediatric Gastroenterology and Solid Organ Transplant, Mayo Clinic, Rochester, Minn. "These findings support the need for ongoing Kanuma treatment in pediatric and adult patients with LAL-D, who historically have faced progressive and life-threatening complications in the absence of an effective therapy."

The safety profile of Kanuma during the extended open-label period, as described above, was consistent with that observed in the double-blind period.

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.[6] In an observational study, approximately 50 percent of children and adults with LAL-D

progressed to fibrosis, cirrhosis, or liver transplant in 3 years.[7] The median age of onset of LAL-D is 5.8 years, and the disease can be diagnosed with a simple blood test.[8,9]

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 replacing the missing vital enzyme and 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 normal development. Kanuma treatment in children and adults led to rapid and significant reductions in ALT and liver fat content, as well as significant improvements in lipid parameters, which were sustained with long-term treatment.

Kanuma is approved in the United States, European Union, and Japan. For its innovation in treating patients with LAL-D, Kanuma received the prestigious 2016 German Prix Galien Award in the Orphan Product category.

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 is the global leader in complement inhibition and has developed and commercializes 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. In addition, Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). 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, 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 June 30, 2016 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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