New Long-Term Data Presented at WCPGHAN 2016 Show Rapid and Sustained Improvements in Important Markers of Liver Injury and Lipid Abnormalities in Children and Adults with Lysosomal Acid Lipase Deficiency (LAL-D) Treated with Kanuma® (sebelipase alfa)

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--Achieved Rapid and Sustained Reduction in ALT, a Marker of Liver Injury, in 97 Percent of Kanuma-Treated Patients with LAL-D, including Higher Proportion of Patients Achieving ALT Normalization at 52 Weeks--

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) announced today that researchers presented new long-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. At 52 weeks of Kanuma treatment, nearly all patients (97 percent) who had received Kanuma from the start of the double-blind period had a rapid and sustained reduction in alanine aminotransferase (ALT), with a mean percent reduction of 53 percent, and an increase from 31 percent (11/36) to 45 percent of patients (15/33) achieving ALT normalization. Similarly, after 52 weeks of Kanuma treatment, nearly all patients (97 percent) who had initially received placebo during the double-blind period had a reduction in ALT, with a mean percent reduction of 52 percent, and 48 percent of patients (14/29) achieving ALT normalization.[1] Sustained improvements were also observed in both groups in markers of lipid abnormalities (including LDL cholesterol, non-HDL cholesterol, triglycerides, and HDL cholesterol) through 52 weeks of Kanuma treatment. These data were reported in a poster presentation at the 5th World Congress of Pediatric Gastroenterology, Hepatology and Nutrition (WCPGHAN) in Montréal, Canada.

"LAL-D is a devastating and progressive disease that can lead to potentially life-threatening consequences, including cirrhosis and severe dyslipidemia," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "Data from the open-label extension of the ARISE study show sustained improvements in several key disease markers and demonstrate that continued treatment with Kanuma for 52 weeks enabled a greater percentage of patients to achieve ALT normalization compared with the initial 20-week period. These long-term results reinforce the benefits of ongoing treatment with the first and only approved therapy for patients with LAL-D."

LAL-D is a genetic, chronic and progressive ultra-rare metabolic disease associated with significant morbidity and premature mortality.[2] Ultra-rare diseases are defined as diseases that affect fewer than 20 patients per 1 million of the general population.[3] 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 rapidly 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.[2,4]

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

Long-term Benefit of Sebelipase Alfa Over 52 Weeks in Children and Adults With Lysosomal Acid Lipase Deficiency (ARISE Trial)[1]

In a poster session, 52-week data were presented 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. Findings from the 20-week, double-blind, randomized, placebo-controlled period of the study (N=66) were published in the *New England Journal of Medicine* in September 2015, and showed that Kanuma was associated with a significantly greater proportion of patients achieving ALT normalization compared with placebo (31 percent vs. 7 percent, p=0.03).[5] Normalization was defined in the trial as ALT below the age- and gender-specific upper limit of normal provided by the central laboratory performing the assay. One hundred percent of Kanuma-treated patients had a reduction in ALT at 20 weeks with a mean percent reduction of 53 percent. This compares with 63 percent of placebo patients who had a reduction in ALT at 20 weeks, with a mean percent reduction of 6 percent. At 20 weeks, patients treated with Kanuma also showed significant improvement versus placebo in six secondary endpoints, including change in LDL cholesterol, change in non-HDL cholesterol, AST normalization, change in triglycerides, change in HDL cholesterol, and change in hepatic fat content.

Sixty-five patients began the open-label portion of the study (ages 4-58 years; median age of 13 years) and were treated with Kanuma for up to 130 weeks, including 35 patients previously treated with Kanuma and 30 previously treated with placebo during the double-blind period. For both groups, efficacy assessments were measured at 52 weeks of Kanuma exposure, except for liver fat content and liver volume, which were measured at a fixed time-point of 52 weeks, reflecting 30 weeks of Kanuma exposure for patients initially treated with placebo and 52 weeks of Kanuma exposure for patients initially treated with Kanuma.

After 52 weeks of Kanuma exposure, 47 percent (29/62) of patients achieved ALT normalization and 56 percent (33/59) of patients achieved aspartate aminotransferase (AST) normalization. Patients also had improvements in lipid abnormalities, including mean LDL cholesterol, non-HDL cholesterol, triglycerides, and HDL cholesterol. Across all measures, results after 52 weeks of treatment with Kanuma were similar for patients previously treated with Kanuma during the double-blind period and patients treated with placebo during the double-blind period. In addition, at a fixed time-point of 52 weeks, hepatic fat content was reduced by a mean of 21.9 percent for patients initially treated with Kanuma and by 28.1 percent for patients initially treated with placebo. Liver volume was reduced by a mean of 13.5 percent for patients initially treated with Kanuma and by 11.4 percent for patients initially treated with placebo.

"We are encouraged by these study results, which show marked and sustained improvements in disease-related lipid and liver abnormalities in

patients with LAL-D who were treated with Kanuma and highlight the need for long-term therapy for patients with this devastating and life-threatening disease," said study investigator Katryn Furuya, M.D., Associate Professor of Pediatrics, Division of Pediatric Gastroenterology and Solid Organ Transplant, Mayo Clinic, Rochester, Minn. "Importantly, results for patients who initially received placebo before switching to Kanuma mirrored those of patients who received Kanuma from the start of the double-blind period, suggesting a consistent and reproducible treatment effect across a large group of treated patients."

The safety profile of Kanuma during the extended open-label period was consistent with that observed in the double-blind period. Most treatment-emergent adverse events (TEAEs) were mild to moderate in severity, and no patient discontinued the open-label study because of adverse events. The most common TEAEs in the open-label period were headache (40 percent), nasopharyngitis (35 percent), and cough (28 percent). Twelve patients (18 percent) experienced an infusion-associated reaction during the open-label period; all but one reaction were mild or moderate in intensity.

Additional Data Presented at WCPGHAN

Researchers are also presenting updated results from the ongoing, open-label, Phase 2/3 VITAL study of Kanuma in infant patients who presented with evidence of growth failure or rapidly progressive LAL-D within the first 6 months of life. Findings were previously reported at the 12th Annual WORLD*Symposium* ™in March 2016, demonstrating that as of January 2016, 5 of 9 patients (56 percent) treated with Kanuma had survived beyond two years of age. New data being presented at WCPGHAN show that as of August 2016, 5 of 9 Kanuma-treated infants had survived beyond three years of age, with the oldest patient now more than five years old. All five patients continue to receive treatment.[6]

Alexion will also present information on the first global LAL-D registry, which aims to improve patient outcomes through a better understanding of the treatment and care of this ultra-rare disease. The registry collects long-term, real-world data on the epidemiology of LAL-D, as well as patient outcomes data.[7]

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.[2] 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.[2,4]

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.[8] In an observational study, approximately 50 percent of children and adults with LAL-D progressed to fibrosis, cirrhosis, or liver transplant in 3 years.[9] The median age of onset of LAL-D is 5.8 years, and the disease can be diagnosed with a simple blood test.[10,11]

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, European Union, and Japan.

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.

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