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New Interim Data Presented at NASPGHAN 2017 Meeting Show Survival Beyond 1 Year of Age in Infants with LAL-D Treated with Kanuma® (sebelipase alfa)

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ: ALXN) announced today that new interim data show that 80% of infants (8 out of 10) with rapidly progressive lysosomal acid lipase deficiency (LAL-D) treated with Kanuma® (sebelipase alfa) survived beyond 1 year of age.[1] Patients also benefited from improvements in a number of key parameters including weight gain and lipid biomarker levels. There were no discontinuations due to adverse events. These data from an ongoing, open-label study were presented at the NASPGHAN Annual Meeting in Las Vegas and confirm previously published survival data from the VITAL study.[2]

"Prior to the availability of Kanuma® the vast majority of infants with rapidly progressive LAL-D did not survive to their first birthday," said John Orloff, M.D., Executive Vice President and Global Head of R&D at Alexion. "We are humbled to see that many of these young children are surviving when treated with Kanuma and also experiencing meaningful improvements in their disease symptoms."

LAL-D is a genetic, chronic and progressive ultra-rare metabolic disease in which patients can suffer from multi-organ damage and experience premature death.[3,4] For LAL-D patients with symptoms presenting in infancy, the median age of death is 3.7 months and mortality by 1 year is nearly 100 percent.[5] LAL-D is caused by genetic mutations that result in a deficiency in LAL enzyme activity in the lysosomes that is vital for the breakdown of lipids, leading to the chronic build-up of lipids (cholesteryl esters and triglycerides) in the liver, blood vessel walls, the intestinal system and other organs.[3,4] Kanuma® replaces the lacking or deficient LAL enzyme and is the only approved therapy to address the underlying cause of LAL-D.[6]

Survival of Infants with Rapidly Progressive Lysosomal Acid Lipase Deficiency Treated with Kanuma®[1]

The current analyses evaluated patient survival and the clinical profile of infants surviving to more than 1 year of age in an ongoing, open-label study of Kanuma® in infants who presented with signs or symptoms of rapidly progressive LAL-D. All 10 patients initiated treatment with Kanuma® prior to 8 months of age and received 1 mg/kg once-weekly. One patient died at 5 months of age after receiving 4 infusions, and another at 13.8 months of age; both causes of death were considered by investigators to be unrelated to treatment with Kanuma®. The 9 patients who survived to 12 months of age had a dose increase to at least 3 mg/kg once-weekly following protocol-defined criteria. As of August 2017, all 8 of the surviving patients are older than 12 months (median age of 29.8 months [range, 16.5-39.4]). The oldest patient has been receiving treatment with Kanuma® for nearly three years (35.8 months).

Clinical Trial Results in Detail:

- Survival: the Kaplan-Meier estimate of survival to 12 months of age was 90 percent.
- Weight gain: patients' weight, as measured by percentiles in the World Health Organization (WHO) growth chart of the general population, ranged from 7.6 to 91.2 at week 48. The median weight-for-age percentile increased from 0.15 at baseline to 37.8 at week 48; this calculates to a median percentile increase of 27.2 from baseline, indicating that the patients´ growth is significantly improving.
- Lipid biomarker levels: Median low-density lipoprotein cholesterol (LDL-C) level was 118.8 mg/dL at baseline and changed by a median of -47.5 percent at week 48 (2 patients), and median high-density lipoprotein cholesterol (HDL-C) was 9.4 mg/dL at baseline and changed by a median of 33.3 percent at week 49 (3 patients).
- Markers of liver disease and hematological disease impact: median ALT level, a measure of liver injury, was 37 U/L at baseline and did not change by week 48 (median percentage change, 0 percent [7 patients]), and median AST, also a measure of liver injury, was 99.5 U/L at baseline and changed by a median of -35.3 percent (6 patients) at week 48. Median albumin level, a measure of synthetic liver function, was 20 g/L at baseline and increased by a median of 30 percent at week 48 (7 patients), median hemoglobin was 90 g/L and increased by a median of 21.7 percent (5 patients), and median platelet count was 146/µL and increased by a median of 54.3 percent at week 48 (5 patients).

All patients experienced one or more treatment emergent adverse events (TEAEs). Six patients experienced serious adverse events that were considered related to sebelipase alfa; all resolved, and there were no discontinuations due to adverse events.

About Lysosomal Acid Lipase Deficiency (LAL-D)

LAL-D is a genetic, chronic, progressive and potentially life-threatening, yet underdiagnosed, ultra-rare disease associated with significant morbidity and premature mortality.[4] In patients with LAL-D, deficient LAL enzyme activity leads to marked accumulation of lipids (cholesteryl esters and triglycerides) in vital organs, blood vessels, and other tissues, resulting in rapid and progressive and multi-organ damage including liver fibrosis and cirrhosis, liver failure, accelerated atherosclerosis, cardiovascular disease, and, in some cases, death or other devastating consequences.[3,4]

LAL-D affects patients of all ages and symptoms may manifest at any time from infancy through adulthood. For LAL-D patients with symptoms presenting in infancy, the median age of death is 3.7 months and mortality by 12 months is nearly 100 percent.[5] For those who develop symptoms as children or adults, approximately 50 percent progress to liver fibrosis, cirrhosis, or transplant within 3 years.[7] Lack of disease awareness of LAL-D has contributed to inadequate testing rates despite the ability to diagnose LAL-D with a simple blood test.[8]

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 lipid 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 in clinical studies led to rapid and significant reductions in alanine aminotransferase (ALT) and liver fat content, as well as significant improvements in lipid parameters, which were sustained with long-term treatment. Patients treated with Kanuma® have also shown improvements in liver damage (as measured by Ishak fibrosis stage scores).[8]

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.

Consider the risks and benefits of re-administering KANUMA following a severe reaction. Monitor patients, with appropriate resuscitation measures available, if the decision is made to re-administer the product.

Hypersensitivity to Eggs or Egg Products

Patients with a known history of egg allergies were excluded from the clinical trials. Consider the risks and benefits of treatment with KANUMA 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 Pharmaceuticals, Inc. is a global biopharmaceutical company focused on bringing hope to patients and families affected by rare diseases by delivering innovative, life-changing therapies. Alexion developed and commercializes the first and only approved complement inhibitor to treat patients with paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and anti-acetylcholine receptor (AChR) antibody-positive generalized myasthenia gravis (gMG). In addition, Alexion has two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare metabolic disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). As the leader in complement biology for over 20 years, Alexion focuses its research efforts on novel molecules and targets in the complement cascade, and its development efforts on the core therapeutic areas of hematology, nephrology, neurology, and metabolic disorders. This press release and further information about Alexion can be found at: www.alexion.com.

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References

1. Jones S, Vijay S, et al. Survival of infants with rapidly progressive lysosomal acid lipase deficiency treated with sebelipase alfa. Poster presented at the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) Annual Meeting, Las Vegas, NV, November 2, 2017.
2. Orphanet J Rare Dis. 2017 Feb 8;12(1):25. doi: 10.1186/s13023-017-0587-3.
3. Reiner Z, et al. Lysosomal acid lipase deficiency - an under-recognized cause of dyslipidemia and liver dysfunction. Atherosclerosis. 2014;235:21-30.
4. Bernstein DL, et al. Cholesteryl ester storage disease: review of the findings in 135 reported patients with an underdiagnosed disease. J Hepatol. 2013;58:1230-43.
5. Jones SA, et al. Rapid progression and mortality of lysosomal acid lipase deficiency presenting in infants. Genetics in Medicine. 27 August 2015.
6. Kanuma® (sebelipase alfa) Full Prescribing Information.
7. Data on File. Alexion Pharmaceuticals, Inc.
8. Hamilton J, et al. A new method for the measurement of lysosomal acid lipase in dried blood spots using the inhibitor Lalistat 2. Clin Chim Acta. 2012;413:1207-10.
9. Goodman ZD, et al. Change in liver fibrosis in children and adults with lysosomal acid lipase deficiency after 52 weeks of sebelipase alfa (ARISE trial) [AASLD abstract 561]. Hepatology. 2016;64:136-361. doi:10.1002/hep.28797/full.

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