May 15, 2017

Long-term Data Confirm Benefits of Treatment with Strensiq® (asfotase alfa) in Adolescents and Adults with Hypophosphatasia (HPP) Through Five Years

- Patients experienced sustained improvements in physical function, speed, agility, and strength -

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (NASDAQ: ALXN) announced today that researchers presented data showing that the rapid benefits of Strensiq® (asfotase alfa) achieved in adolescents and adults (ages 13-66 years at study entry) with hypophosphatasia (HPP) within the first 6 months were sustained through 5 years of treatment.[1] These are the final data from the extension phase of a randomized, open-label, dose-ranging Phase 2 trial of Strensiq and they confirm previously presented interim results.

The results were presented at the European Calcified Tissue Society (ECTS) Congress in Austria and demonstrate a reduction in two key biomarkers of HPP disease activity, as well as improvements in physical function in patients treated with Strensiq, as observed in tests to measure walking distance, running speed and agility, and muscle strength. Strensiq was generally well-tolerated. The most common treatment-related adverse events were mild to moderate injection-site reactions.[1]

"The findings of this phase 2 study suggest that asfotase alfa appears to be safe and effective long-term and reduces the debilitating burden of HPP in adolescent and adult patients," said lead author, Priya S. Kishnani, M.D., Division Chief, Medical Genetics, Duke University School of Medicine, Durham, North Carolina. "Patients with HPP can suffer multiple fractures, deformities, short stature, impaired mobility, pain, and limited activities of daily living."

Strensiq is approved in the United States as a treatment for patients with perinatal-, infantile- or juvenile-onset HPP. Strensiq is also approved in Australia, Canada, the European Union, Israel, Japan, South Korea, and Switzerland.

Further details of the study results[1]

- Reductions in plasma concentrations of plasma pyridoxal 5' phosphate (PLP) and inorganic pyrophosphate (PPi) levels at 6 months were greater in patients treated with Strensiq than in the control group. PLP and PPi are substrates of the enzyme (tissue non-specific alkaline phosphatase, TNSALP) that patients with HPP lack and that Strensiq replaces. As such, PLP and PPi are biomarkers to measure reduction in HPP disease activity. Decreases from Baseline in both PLP and PPi levels were maintained through 5 years.
- Physical function, as measured by the Six Minute Walk Test (6MWT), improved from a median of 76 percent of that predicted for healthy peers at Baseline (n=15; below normal range) to a median of 85 percent predicted (n=16; within the normal range) by 6 months in patients treated with Strensiq. Results were sustained through 5 years of treatment and increased to 88 percent (n=11) at 5 years.
- Speed and agility, as measured by median change from Baseline in the BOT-2 Running Speed and Agility subscale, increased by a median of 4 points after 5 years of treatment (n=11).
- Strength, as measured by median change from Baseline in the BOT-2 Strength subscale, increased by a median of 3.5 points after 5 years of treatment (n=12).
- 1 patient withdrew because of serious AEs of injection site hypersensitivity and anaphylactoid reaction (1 episode each). This patient subsequently received Strensiq post-marketing without reaction. All patients experienced ≥1 treatment-emergent adverse event (TEAE); the majority of TEAEs were mild in intensity.

In the primary phase of this study, patients were randomized to receive no treatment (n=6), 0.3 mg/kg/day of Strensiq (n=7), or 0.5 mg/kg/day of Strensiq (n=6) for 6 months. The majority of patients (with the exception of 1 adult patient) had confirmed pediatric-onset HPP. At 6 months, all 19 patients entered the extension phase of the study and were treated with 0.5 mg/kg/day of Strensiq, then changed to 1 mg/kg/day, 6 times a week, over the next 6 to 12 months. Fourteen patients completed the study over 5 years. Data from both Strensiq dosage groups were pooled for the primary analysis.

The approved dosing regimen for patients with perinatal/infantile-onset and juvenile-onset HPP is 2 mg/kg administered subcutaneously three times per week, or 1 mg/kg administered six times per week. (The U.S. Prescribing Information recommends increasing the dose to 3 mg/kg three times per week in patients with infantile-onset HPP in cases of insufficient

efficacy).

About Hypophosphatasia (HPP)

HPP is a genetic, chronic, progressive, and potentially life-threatening ultra-rare metabolic disease that can affect people of all ages. HPP is characterized by defective bone mineralization that can lead to weakness and deformity of bones, fractures and other skeletal abnormalities, as well as systemic complications such as profound muscle weakness, muscle, bone and joint pain, seizures in perinatal/infantile forms of HPP, and respiratory failure leading to premature death in infants.[2-6] HPP is traditionally classified by the age of the patient at the onset of symptoms of the disease, with perinatal-, infantile- and juvenile-onset HPP defined by the onset of the first symptom prior to 18 years of age.

HPP can have devastating consequences for patients at any stage of life.[2] In a natural history study, infants who had their first symptom of HPP within the first 6 months of life had high mortality, with an overall mortality rate of 73 percent at 5 years.[7] In these patients, mortality was primarily due to respiratory failure.[2,6,8] In patients surviving and those with juvenile-onset HPP, long-term clinical sequelae include recurrent and non-healing fractures, profound muscle weakness, debilitating pain, and the requirement for ambulatory assistive devices such as wheelchairs, wheeled walkers and canes.[2,5]

HPP is caused by mutations in the gene encoding an enzyme known as tissue non-specific alkaline phosphatase (TNSALP). This enzyme plays a critical role in the proper mineralization of bones.[2,3]

About Strensiq® (asfotase alfa)

Strensiq® (asfotase alfa) is a highly innovative bone-targeted enzyme replacement therapy that treats the underlying cause of HPP by replacing the missing TNSALP enzyme. In clinical studies of patients with HPP who had their first symptom prior to the age of 18, treatment with Strensiq improved overall survival in infants, enhanced bone mineralization and improved height, weight and mobility.

Strensiq is approved in Australia, Canada, the European Union, Israel, Japan, South Korea, and Switzerland, and the United States.

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions, including anaphylaxis, have been reported in STRENSIQ-treated patients. Signs and symptoms consistent with anaphylaxis included difficulty breathing, choking sensation, nausea, periorbital edema, and dizziness. These reactions have occurred within minutes after subcutaneous administration of STRENSIQ and can occur in patients on treatment for more than one year. Other hypersensitivity reactions have also been reported in STRENSIQ-treated patients, including vomiting, fever, headache, flushing, irritability, chills, skin erythema, rash, pruritus and oral hypoesthesia. If a severe hypersensitivity reaction occurs, discontinue STRENSIQ treatment and initiate appropriate medical treatment. Consider the risks and benefits of re-administering STRENSIQ to individual patients following a severe reaction. If the decision is made to re-administer the product, monitor patients for a reoccurrence of signs and symptoms of a severe hypersensitivity reaction.

Localized lipodystrophy, including lipoatrophy and lipohypertrophy, has been reported at injection sites after several months in patients treated with STRENSIQ. Advise patients to follow proper injection technique and to rotate injection sites.

Patients with HPP are at increased risk for developing ectopic calcifications. In clinical trials, 14 cases (14%) of ectopic calcification of the eye, including the cornea and conjunctiva, and the kidneys (nephrocalcinosis) were reported. There was insufficient information to determine whether or not the reported events were consistent with the disease or due to STRENSIQ. No visual changes or changes in renal function were reported. Ophthalmology examinations and renal ultrasounds are recommended at baseline and periodically during treatment with STRENSIQ to monitor for signs and symptoms of ophthalmic and renal ectopic calcifications and for changes in vision or renal function. The most common adverse reactions (≥ 10%) are injection site reactions, lipodystrophy, ectopic calcifications and hypersensitivity reactions.

Please click here for the full Prescribing Information.[9]

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 its rare disease pipeline 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 Strensiq® (asfotase alfa) for hypophosphatasia (HPP). 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 the adequacy of our research, marketing approval or material limitations on the marketing of Strensiq for HPP, delays in arranging satisfactory manufacturing capabilities and establishing commercial infrastructure for Strensiq for HPP, the possibility that results of clinical trials are not predictive of safety and efficacy results of Strensiq in broader or different patient populations, the adequacy of our pharmacovigilance and drug safety reporting processes, the risk that estimates regarding the number of patients with Strensiq and observations regarding the natural history of patients with Strensiq 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 March 31, 2017 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

1. Kishnani P, Rockman-Greenberg, C, Denker A, et al. Biochemical and Physical Function Outcomes in Adolescents and Adults With Hypophosphatasia Treated With Asfotase Alfa for 5 Years: Results From a Phase 2 Study. Poster presented at the European Calcified Tissue Society Congress, Salzburg, Austria, May 15, 2016.

2. Rockman-Greenberg C. Hypophosphatasia. *Pediatr Endocrinol Rev*. 2013; 10(suppl 2):380-388.

3. Whyte MP. Hypophosphatasia: nature's window on alkaline phosphatase function in humans. In: Bilezikian JP, Raisz LG, Martin TJ, eds. Principles of Bone Biology. Vol 1. 3rd ed. San Diego, CA: Academic Press; 2008:1573-1598.

4. Whyte MP, Greenberg CR, Salman N, et al. Enzyme-replacement therapy in life-threatening hypophosphatasia. *N Engl J Med.* 2012; 366(10):904-913.

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6. Baumgartner-Sigl S, Haberlandt E, Mumm S, et al. Pyridoxine-responsive seizures as the first symptom of infantile hypophosphatasia caused by two novel missense mutations (c.677T > C, p.M226T; c.1112C > T, p.T371I) of the tissue-nonspecific alkaline phosphatase gene. *Bone*. 2007; 40(6):1655-1661.

7. Whyte MP, Leung E, Wilcox W, et al. Hypophosphatasia: a retrospective natural history study of the severe perinatal and infantile forms. Poster presented at the 2014 Pediatric Academic Societies and Asian Society for Pediatric Research Joint Meeting, Vancouver, B.C., Canada, May 5, 2014. Abstract 752416.

8. Whyte MP, Rockman-Greenberg C, Hofmann C, et al. Improved survival with asfotase alfa treatment in pediatric patients with hypophosphatasia at high risk of death. Poster presented at the American Society for Bone and Mineral Research (ASBMR) 2014 Annual Meeting, Houston, September 14, 2014. Abstract 1097.

9. U.S. Prescribing Information for STRENSIQ® (asfotase alfa)

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