Asfotase Alfa Significantly Decreased TNSALP Substrates and Improved 6-Minute Walk Test Results in Adolescents and Adults with Hypophosphatasia (HPP)

Data from Phase 2 Study Presented at the American College of Medical Genetics (ACMG) Annual Meeting

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) today announced data from a Phase 2 study of asfotase alfa in adolescents and adults with hypophosphatasia (HPP), a severe and ultra-rare metabolic disorder. In the study, all patients who were treated with asfotase alfa had an objective response to therapy as indicated by a reduction in tissue non-specific alkaline phosphatase (TNSALP) substrates. In addition, treated patients demonstrated improvement in the six-minute walk test (6MWT). Asfotase alfa is an investigational therapy being developed by Alexion as a potential treatment for patients with HPP. Data were presented today at the American College of Medical Genetics (ACMG) Annual Clinical Genetics Meeting, being held March 27-31 in Charlotte, NC.

"HPP is a devastating disease that affects people of all ages, and patients can experience debilitating systemic complications that can be life-threatening," said study author Priya Kishnani, M.D., Professor of Pediatrics and Division Chief of Medical Genetics at Duke University Medical Center. "Asfotase alfa is the first treatment designed to target the underlying mechanism of HPP. In this study, asfotase alfa showed a positive impact on adolescents and adults with HPP by significantly decreasing the two key TNSALP substrates that accumulate in HPP and are key indicators of disease activity. Importantly, from a clinical perspective, patients experienced improved function in the six-minute walk test, a standard measure of functional capacity."

About HPP and Asfotase Alfa

HPP is an ultra-rare, inherited, life-threatening metabolic disease affecting patients of all ages for which there are currently no approved or effective treatment options. Patients with HPP have an inborn error of metabolism resulting from a genetic, life-long deficiency of the enzyme known as TNSALP. This lack of TNSALP leads to accumulation of substrates, causing abnormalities in calcium and phosphate regulation, which can result in progressive damage to multiple vital organs, destruction and deformity of bones, profound muscle weakness, impaired renal function and respiratory failure.[1,2,3,4] In addition, infants with HPP may experience seizures, and approximately 50 percent of infants with severe disease do not survive past one year of age.[1,5]

Asfotase alfa is an investigational, highly innovative, first-in-class targeted enzyme replacement therapy designed to address the underlying cause of HPP by targeting replacement of the missing enzyme to the necessary body tissues. Asfotase alfa is designed to normalize the genetically defective metabolic process and prevent or reverse the severe and life-threatening complications of life-long uncontrolled mineral metabolism in patients with HPP.

About the Study

The open-label, multicenter, randomized, controlled, Phase 2 study enrolled 19 adolescent and adult patients with HPP. Patients in the study were between the ages of 14 and 68 years old, with an average age of 42 years. Thirteen patients in the study received daily asfotase alfa subcutaneous injections in one of two dose cohorts (2.1 mg/kg/week (N=7) or 3.5 mg/kg/week (N=6)), while six patients received no treatment. The primary objective of the study was to evaluate the effect of asfotase alfa on TNSALP substrate levels and secondary objectives included assessments of changes in 6MWT following 24 weeks of treatment.

The study achieved its primary endpoint, as treatment with asfotase alfa was associated with statistically and clinically significant reductions in the two measured TNSALP substrates, PPi (inorganic pyrophosphate) and PLP (pyridoxal 5' phosphate). PPi has several functions, including the inhibition of mineralization. Asfotase alfa treatment was associated with a significant reduction in PPi at 24 weeks in the combined treatment groups compared to the untreated cohort (p=0.002). Asfotase alfa treatment was associated with a decrease in PPi from 5.5 µM (± 1.51) at baseline to 3.5 µM (± 0.49) at Week 24 in the lower dose cohort and from 5.0 µM (± 1.84) at baseline to 2.8 µM (± 1.44) in the higher dose cohort. Asfotase alfa treatment was also associated with significant reductions in PLP at 24 weeks in the combined treatment groups compared to the untreated cohort (p=0.009). Asfotase alfa treatment was associated with a decrease in PLP from 324 ng/mL (±254) at baseline to 69 ng/mL (± 80) at 24 weeks in the lower dose cohort group and from 603 ng/mL (± 660) to 38 ng/mL (± 45) in the higher dose cohort.

Functional capacity, as measured by the 6MWT, improved in patients treated with asfotase alfa. At baseline, patients had an average distance walked of 349 meters (range of 6-620 meters), with 10 of the 19 patients requiring assistive devices to complete the test. Patients treated with asfotase alfa had an average improvement of 26 meters walked, while the untreated patients had an average decrease from baseline of 14 meters walked at 24 weeks. In treated patients who had a baseline 6MWT between 25% and 75% of normal for their age (9 out of 13 patients), mean improvement in 6MWT at 24 weeks was 35 meters in the lower dose cohort (n=5) and 44 meters in the higher dose cohort (n=4).

The most common treatment-related adverse events observed in the study were injection site erythema, pain in extremities and arthralgia (joint pain). There were three serious adverse events in two of the 13 patients treated with asfotase alfa; all three were deemed to be unrelated to asfotase alfa. In addition, there were four serious adverse events in two of six patients in the no treatment cohort.

"Following the recent publication of strong data from our study of asfotase alfa treatment of infants with HPP, this study now indicates the positive impact that asfotase alfa may have on adult and adolescent patients suffering with HPP," said Leonard Bell, M.D., Chief Executive Officer of Alexion. "We are continuing to drive the development of asfotase alfa as a treatment for HPP patients of all ages. As our pediatric program continues, our expanding adult program will be further informed by the encouraging results of this study."

About Alexion

Alexion Pharmaceuticals, Inc. is a biopharmaceutical company focused on serving patients with severe and ultra-rare disorders through the innovation, development and commercialization of life-transforming therapeutic products. Alexion is the global leader in complement inhibition, and has developed and markets Soliris® (eculizumab) as a treatment for patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is currently approved in more than 35 countries for the treatment of PNH, and in the United States and the European Union for the treatment of aHUS. Alexion is evaluating other potential indications for Soliris and is developing four other highly innovative biotechnology product candidates, including asfotase alfa. This press release and further information about Alexion Pharmaceuticals, Inc. can be found at: www.alexionpharma.com.

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Safe Harbor Statement

This news release contains forward-looking statements, including statements related to potential medical benefits of 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, decisions of regulatory authorities regarding marketing approval or material limitations on the marketing of asfotase alfa for HPP, delays in arranging satisfactory manufacturing capabilities and establishing commercial infrastructure for asfotase alfa for HPP, the possibility that results of clinical trials are not predictive of safety and efficacy results of asfotase alfa in broader or different patient populations, the risk that third party payors (including governmental agencies) will not reimburse for the use of asfotase alfa (if approved) at acceptable rates or at all, the risk that estimates regarding the number of patients with asfotase alfa and observations regarding the natural history of patients with asfotase alfa 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 year ended December 31, 2011 and in our other filings with the Securities and Exchange Commission. 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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