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New Data Evaluating Asfotase Alfa in Infants and Young Children with Hypophosphatasia (HPP) Presented at Paediatric Endocrinology Meeting

- Early and Continued Improvement in Skeletal Mineralization Observed with 93% Survival in Studied Patients -

- Patients Also Improved or Preserved Respiratory Function -

CHESHIRE, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) today announced that researchers have presented data from an ongoing multinational Phase 2 study of asfotase alfa in infants and young children with hypophosphatasia (HPP), an inherited, ultra-rare metabolic disorder that in this patient population leads to progressive damage to multiple vital organs, destruction and deformity of bones, and death. The study met its primary endpoint: infants and young children with HPP treated with asfotase alfa had significant improvement in skeletal mineralization from baseline as assessed radiographically after 24 weeks of treatment ($p=0.001$). This response was observed as early as 12 weeks and improvement continued at 48 weeks. Ninety three percent of the patients survived the first 48 weeks of treatment with 80% of patients having improved respiratory status or requiring no respiratory support at the final analysis. The data were presented in a late-breaking presentation at the 9th Joint Meeting of Paediatric Endocrinology in Milan, Italy.¹

"Hypophosphatasia is a genetic, very rare metabolic disease that can have devastating and life-threatening consequences. HPP is characterized by profound hypomineralization and a number of systemic effects, including respiratory, neurologic and renal complications. Infants who develop their first symptoms of HPP before 6 months of age have a very poor prognosis with an estimated 50% mortality rate," said lead investigator Dr. Cheryl R. Greenberg, of the University of Manitoba in Winnipeg, Canada. "This study showed that treatment with asfotase alfa improved bone mineralization in infants and young children with HPP, and improved or preserved respiratory function, which is often a cause of death in these patients."

"We are excited about these results as they are consistent with previously reported positive data now in a broader patient population of infants and children," said Martin Mackay, Ph.D. Executive Vice President, Global Head of R&D at Alexion. "This further supports the potential of asfotase alfa as the first treatment for HPP, and we look forward to completing our registration program so that we may begin serving patients with this severe and often life-threatening disease."

Alexion is developing asfotase alfa as a potential treatment for HPP. Asfotase alfa was used on an investigational basis in the reported study. The U.S. Food and Drug Administration (FDA) recently designated asfotase alfa a Breakthrough Therapy for the treatment of patients with HPP whose first signs or symptoms occurred prior to 18 years of age, including perinatal-, infantile-, and juvenile-onset forms of the disease.

About the Phase 2 Trial of Asfotase Alfa in HPP

Results were presented from an ongoing multinational, Phase 2, open-label study that enrolled 15 infants and children with HPP (age 5 years or younger) representing a range of HPP characteristics; of this number, 13 patients were included in the Week 24 primary analysis. The median patient age at baseline was 21.14 weeks (range: 0.1-304.0 weeks), and all patients had experienced symptoms of HPP prior to 6 months old.¹

The primary efficacy endpoint of the study was change in skeletal manifestations of HPP over time. The analysis presented today measured this endpoint as changes in the severity of rickets (softening and weakening of bones, which is unrelated to nutrition in patients with HPP) from baseline to Week 24, as assessed by the Radiographic Global Impression of Change (RGI-C) scale, a 7-point scale in which a rating of -3 represents severe worsening and a rating of +3 indicates near or complete healing. Response to treatment was defined as change from baseline in RGI-C of two or more points. Secondary endpoints included changes in respiratory support status, overall survival, and safety and tolerability.

Interim results presented today showed that the 13 evaluable patients treated with asfotase alfa had a significant improvement from baseline to Week 24 in skeletal mineralization, with a mean (standard deviation) increase in RGI-C score of 1.74 (1.107) and a median increase of 2.00 ($p=0.001$). Response to asfotase alfa therapy was evident as early as 12 weeks, with improvement continuing to Week 48. Eight of 12 evaluable patients were characterized as responders (defined as an RGI-C score of +2 [substantial healing] or greater) at Week 24, and all 10 of the evaluable patients at Week 48 were responders. Three patients had RGI-C scores of +3, which indicate near complete healing, at both Weeks 24 and 48.¹

Additionally, the majority of patients (12/15) treated with asfotase alfa improved or preserved respiratory function. Among the

eight patients who required respiratory support during the trial, five had improved by their last assessment, and four patients no longer required any support. The overall survival rate, another secondary endpoint, at 48 weeks was 93%. One patient in the study withdrew consent after receiving two doses of asfotase alfa; this patient later died from disease-related complications; the patient's death was deemed unrelated to the study drug.¹

Asfotase alfa was well-tolerated in the study with no deaths, serious adverse events or discontinuations of therapy deemed related to treatment. The most common adverse events were mild to moderate injection site reactions, reported in 10 of the 15 patients (66.7%). These reactions included redness, (46.7%), discoloration, (26.7%), and hardening of the skin (13.3%). The trial continues to enroll patients and patients continue on treatment.¹

About Hypophosphatasia (HPP)

HPP is a chronic, life-threatening, genetic, and ultra-rare metabolic disease characterized by defective bone mineralization and impaired phosphate and calcium regulation that can lead to progressive damage to multiple vital organs including destruction and deformity of bones, profound muscle weakness, seizures, impaired renal function, and respiratory failure.³⁻⁶

HPP is caused by a genetic deficiency of an enzyme known as tissue non-specific alkaline phosphatase (TNSALP), which causes life-long abnormalities in metabolism of two minerals, calcium and phosphate, leading directly to the debilitating morbidities and premature mortality of the disease.³

The genetic deficiency in HPP can affect people of all ages.³ HPP is traditionally classified by the age of the patient at the onset of the disease. Patients with perinatal-onset HPP manifest their first signs of disease in utero or at birth. This form of the disease is usually lethal and often leads to death in utero. Those patients who survive birth often have severely compromised respiratory function.⁷

Patients with infantile-onset HPP develop their first signs or symptoms of HPP before 6 months of age. Individuals with this form of disease develop skeletal abnormalities and may present with failure to thrive and respiratory failure within the first 6 months of post-natal life. The prognosis of these patients is very poor with mortality estimated at 50%.³

Patients with juvenile-onset HPP exhibit their first signs or symptoms of HPP after 6 months of age and before 18 years of age. Individuals with this form of the disease are at risk for respiratory complications, painful fractures, and profound muscle weakness and can have delayed acquisition of age-appropriate motor skills due to hypo-mineralization and muscle weakness leading to need for walking assistance; some may never walk.³

About Asfotase Alfa

Asfotase alfa is an investigational, highly innovative, first-in-class targeted enzyme replacement therapy. Asfotase alfa is designed to address the underlying cause of HPP by normalizing the genetically defective metabolic process, and preventing or reversing the severe and potentially life-threatening complications of life-long dysregulated mineral metabolism.

According to the FDA, a Breakthrough Therapy designation is designed to expedite the development of a drug to treat a serious or life-threatening disease when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The Breakthrough Therapy designation is part of the FDA Safety and Innovation Act (FDASIA) of 2012.⁸

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 PNH and aHUS, two debilitating, ultra-rare and life-threatening disorders caused by chronic uncontrolled complement activation. Soliris is currently approved in more than 40 countries for the treatment of PNH, and in the United States, Europe, Japan and other territories for the treatment of aHUS. Alexion is evaluating other potential indications for Soliris and is pursuing development of four other innovative biotechnology product candidates which are being investigated across additional severe and ultra-rare disorders beyond PNH and aHUS. 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 Quarterly Report on Form 10-Q for the period ended June 30, 2013. 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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