



## Horizon Pharma plc Presents Results from an Open-Label Study on the Use of PROCYSBI® (cysteamine bitartrate) Delayed-Release Capsules in Treatment-Naïve Children Younger than 6 Years of Age

November 4, 2017

DUBLIN, Ireland, Nov. 04, 2017 (GLOBE NEWSWIRE) -- Horizon Pharma plc (NASDAQ:HZNP), a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs, today announced results from a new open-label study evaluating the effects of PROCYSBI® (cysteamine bitartrate) delayed-release capsules in treatment-naïve children younger than 6 years of age living with nephropathic cystinosis. These data were presented at the American Society of Nephrology (ASN) Kidney Week 2017 Annual Meeting in New Orleans on Saturday, Nov. 4. In the United States, PROCYSBI is a cystine depleting agent indicated for the treatment of nephropathic cystinosis in adults and pediatric patients two years of age and older.

In the study, children enrolled achieved lowered and prolonged maintenance of white blood cell (WBC) cystine levels – the biomarker for disease control – over the course of one year of therapy. Additionally, they experienced measured improvements in height, weight and body surface area (BSA).

"Nephropathic cystinosis is typically diagnosed in children at a young age, and the importance of early, continuous cystine depleting therapy, as evidenced by control of WBC cystine levels, cannot be overstated – we know that repetitive missed doses of cystine depleting therapy can damage cells, tissues and organs throughout the body," said Craig B. Langman, M.D., lead investigator for the study, head of kidney diseases and the Isaac A. Abt MD professor of kidney diseases, The Ann and Robert H. Lurie Children's Hospital of Chicago, as well as professor of pediatrics at Northwestern University Feinberg School of Medicine. "These results are exciting because children enrolled in the study who had not previously been treated with cysteamine therapy were able to obtain and maintain target WBC cystine levels with PROCYSBI and reach several growth milestones equal to standard measures for unaffected children of the same age."

### Summary of Study Results:

- This long-term (minimum of 12 months), prospective, controlled, open-label study enrolled 17 people living with nephropathic cystinosis, including 15 children between the ages of 1 and 4.5 (mean age: 2.2 years).
- The primary objective was to determine the long-term safety and effectiveness of PROCYSBI on WBC cystine levels among patients naïve to prior cysteamine treatment.
- The percentage of patients who reached WBC cystine levels of less than 1.0 nmol ½ cystine/mg increased over the treatment period.
- While the study was not designed to evaluate changes in height, weight, and body surface area, the results support further investigation of the effect of PROCYSBI on these measures. Mean height, weight and BSA increased over the treatment period.
  - Mean height was in the 2.59 percentile ( $\pm 4.00$ ) of the reference population on Day 1 and rose to the 50.52 ( $\pm 40.46$ ) percentile at Study Exit.
  - Mean weight was in the 3.46 percentile ( $\pm 11.13$ ) of the reference population on Day 1 and rose to the 32.85 ( $\pm 35.58$ ) percentile at Study Exit.
  - Mean BSA was in the 10.87 percentile ( $\pm 21.26$ ) of the reference population on Day 1 and rose to the 19.41 ( $\pm 23.96$ ) percentile at Study Exit.
- Mean Body Mass Index (BMI) was relatively unchanged over the treatment period.
  - Mean BMI was in the 22.44 percentile ( $\pm 27.83$ ) of the reference population at Day 1 and in the 21.57 percentile ( $\pm 28.19$ ) at Study Exit.
- The most commonly reported adverse events during the study were upper respiratory tract infection, viral gastroenteritis, vomiting, diarrhea, cough, dehydration and electrolyte imbalance.
- The most common adverse reactions (? 5%) in patients treated in clinical trials reflected in the FDA approved product labeling were vomiting, nausea, abdominal pain, breath odor, diarrhea, skin odor, fatigue, rash and headache.
- This study was required by the U.S. Food and Drug Administration ("FDA") as a post-marketing commitment after PROCYSBI was approved. The results of this study are not included in the FDA approved product labeling for PROCYSBI. PROCYSBI is not approved for use in children less than two years of age.

"Previous PROCYSBI studies evaluated people living with cystinosis who switched to PROCYSBI from immediate-release cysteamine, making this the first time we've had data on treatment-naïve patients," said Jeffrey W. Sherman, M.D., FACP, executive vice president, research and development and chief medical officer, Horizon Pharma plc. "These results add to our research studying the use of PROCYSBI for people living with nephropathic cystinosis, including children during the crucial early years of growth and development."

### Presentation Details:

Title: *Delayed-Release Cysteamine Bitartrate (DR Cysteamine) Controls WBC Cystine Levels and Promotes Growth in Treatment-Naïve Patients < 6 Years of Age with Nephropathic Cystinosis*

Poster #: SA-PO560

Authors:

- Craig B. Langman, M.D., Feinberg School of Medicine, Northwestern University, and The Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, Ill.
- Juliana Caires Ferreira, M.D., Instituto da Criança do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), São Paulo, Brazil
- Kyleen D. Young, APN, The Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, Ill.

- Maria Helena Vaisbich, MD, PhD, Division of Nephrology, São Paulo University Medical School, São Paulo, Brazil

Date: Saturday, Nov. 4

Time: 10 a.m. – 12 p.m. CT

#### About Cystinosis

Nephropathic cystinosis is a rare, life-threatening metabolic lysosomal storage disorder that causes toxic accumulation of cystine in all cells, tissues, and organs in the body. If untreated, elevated cystine accumulation leads to progressive, irreversible tissue damage and multi-organ failure, including kidney failure, blindness, muscle wasting and premature death. It is estimated that only about 2,000 people worldwide are currently diagnosed with nephropathic cystinosis. Nephropathic or "classic infantile" cystinosis – the most common and most severe form of the disease – is typically diagnosed in infancy and requires lifelong cystine depleting therapy.<sup>1</sup>

#### IMPORTANTSAFETYINFORMATION

**INDICATIONS AND USAGE:** PROCYSBI® (cysteamine bitartrate) delayed-release capsules is a cystine depleting agent indicated for the treatment of nephropathic cystinosis in adult and pediatric patients 2 years of age and older.

#### CONTRAINDICATIONS:

- Hypersensitivity to penicillamine or cysteamine.

#### WARNINGSANDPRECAUTIONS:

- Ehlers-Danlos-like Syndrome: Skin and bone lesions that resemble clinical findings for Ehlers-Danlos-like syndrome have been reported in patients treated with high doses of immediate-release cysteamine bitartrate or other cysteamine salts.
  - These include molluscoid pseudotumors (purplish hemorrhagic lesions), skin striae, bone lesions (including osteopenia, compression fractures, scoliosis and genu valgum), leg pain and joint hyperextension.
  - One patient on immediate-release cysteamine bitartrate with serious skin lesions subsequently died of acute cerebral ischemia with marked vasculopathy.
  - Patients should be monitored for development of skin or bone lesions and PROCYSBI dosing should be interrupted if patients develop these lesions. PROCYSBI may be restarted at a lower dose under close supervision, then slowly increased to the appropriate therapeutic dose.
- Skin Rash: Severe skin rashes such as erythema multiforme bullosa or toxic epidermal necrolysis have been reported in patients receiving immediate-release cysteamine bitartrate. If severe skin rashes develop, use of PROCYSBI should be permanently discontinued.
- Gastrointestinal Ulcers and Bleeding: Gastrointestinal (GI) ulceration and bleeding have been reported in patients receiving immediate-release cysteamine bitartrate.
  - GI tract symptoms including nausea, vomiting, anorexia and abdominal pain, sometimes severe, have been associated with cysteamine. If severe GI tract symptoms develop, decreasing the dose of PROCYSBI should be considered.
- Central Nervous System Symptoms: Central Nervous System (CNS) symptoms such as seizures, lethargy, somnolence, depression, and encephalopathy have been associated with immediate-release cysteamine.
  - Neurological complications have also been described in some patients with cystinosis who have not been treated with cysteamine.
  - Patients who develop CNS symptoms should be carefully evaluated and monitored. Medication should be interrupted or the dose should be adjusted as necessary for patients with severe symptoms or with symptoms that persist or progress.
  - PROCYSBI may impair the ability of patients to perform tasks such as driving or operating machinery.
- Leukopenia and/or Elevated Alkaline Phosphatase Levels: Cysteamine has been associated with reversible leukopenia and elevated alkaline phosphatase levels. White blood cell counts and alkaline phosphatase levels should be monitored. If test values remain elevated, consider decreasing the dose or discontinuing the drug until values revert to normal.
- Benign Intracranial Hypertension: Benign intracranial hypertension (pseudotumor cerebri; PTC) and/or papilledema has been reported in patients receiving immediate-release cysteamine bitartrate treatment.
  - Patients should be monitored for signs and symptoms of PTC, including headache, tinnitus, dizziness, nausea, diplopia, blurry vision, loss of vision, pain behind the eye or pain with eye movement. If signs/symptoms persist, dosing should be interrupted or the dose should be decreased and the patient should be referred to an ophthalmologist. If the diagnosis is confirmed, use of PROCYSBI should be permanently discontinued.

#### ADVERSEREACTIONS:

The most common adverse reactions (?5%) in patients treated in clinical trials are vomiting, nausea, abdominal pain, breath odor, diarrhea, skin odor, fatigue, rash and headache.

To reportSUSPECTEDADVERSEREACTIONS, contact HorizonPharma USA, Inc, at1-855-888-4004 orFDAat 1-800-FDA-1088 or[www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### DRUGINTERACTIONS:

- Drugs that Increase Gastric pH: PROCYSBI should be administered at least 1 hour before or 1 hour after medications containing bicarbonate or carbonate.
- Consumption of alcohol with PROCYSBI may increase the rate of cysteamine release and/or adversely alter the pharmacokinetic properties, as well as the effectiveness and safety of PROCYSBI.

- PROCYSBI can be administered with electrolyte (except bicarbonate) and mineral replacements necessary for management of Fanconi Syndrome as well as vitamin D and thyroid hormone.

#### **USEIN SPECIFICPOPULATIONS**

##### **Lactation:**

- Breastfeeding is not recommended while taking PROCYSBI.

##### **Horizon Pharma plc**

Horizon Pharma plc is a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs. The Company markets 11 medicines through its orphan, rheumatology and primary care business units. For more information, please visit [www.horizonpharma.com](http://www.horizonpharma.com). Follow [@HZNPplc](https://twitter.com/HZNPplc) on Twitter, like us on [Facebook](https://www.facebook.com/horizonpharma) or view careers on our [LinkedIn](https://www.linkedin.com/company/horizonpharma) page.

##### **Forward-Looking Statements**

This press release contains forward-looking statements, including statements regarding the potential of PROCYSBI to treat patients with nephropathic cystinosis. These forward-looking statements are based on management expectations and assumptions as of the date of this press release, and actual results may differ materially from those in these forward-looking statements as a result of various factors. These factors include whether patients are willing to use PROCYSBI to treat nephropathic cystinosis and whether use of PROCYSBI outside of the clinical trial setting will demonstrate results consistent with clinical trials, as well as those factors described in Horizon Pharma's filings with the United States Securities and Exchange Commission, including those factors discussed under the caption "Risk Factors" in those filings. Forward-looking statements speak only as of the date of this press release and Horizon Pharma does not undertake any obligation to update or revise these statements, except as may be required by law.

##### **Contacts:**

Tina Ventura  
Senior Vice President, Investor Relations  
[Investor-relations@horizonpharma.com](mailto:Investor-relations@horizonpharma.com)

Ruth Venning  
Executive Director, Investor Relations  
[Investor-relations@horizonpharma.com](mailto:Investor-relations@horizonpharma.com)

##### **U.S. Media Contact:**

Matt Flesch  
Executive Director, Product Communications  
[media@horizonpharma.com](mailto:media@horizonpharma.com)

##### **Ireland Media Contact:**

Ray Gordon  
Gordon MRM  
[ray@gordonmrm.ie](mailto:ray@gordonmrm.ie)

##### **References:**

1. Cystinosis Research Foundation. "About cystinosis." Available at <http://www.cystinosisresearch.org/About-Cystinosis/>. Accessed Nov. 2, 2017.

Source: Horizon Pharma plc