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Horizon Pharma plc Announces Four Poster Presentations on PROCYSBI® (Cysteamine Bitartrate) Delayed-Release Capsules at Cystinosis Research Network 2017 Family Conference

-- In a New Study Comparing PROCYSBI and Immediate-Release Cysteamine, Those Treated with PROCYSBI Had a 26 Percent Reduction in Exhaled Dimethyl Sulphide, Which is Associated with Halitosis --

DUBLIN, Ireland, July 14, 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 the presentation of results from a new study evaluating the effects of treatment with PROCYSBI® (cysteamine bitartrate) delayed-release capsules or immediate-release cysteamine bitartrate on the breath of people living with nephropathic cystinosis. In the study, patients receiving PROCYSBI had a 26 percent reduction in exhaled dimethyl sulphide - a metabolite of cysteamine bitartrate associated with halitosis (i.e., bad breath) - compared to those receiving immediate-release cysteamine. The study is one of four PROCYSBI poster presentations that can be viewed at the Cystinosis Research Network (CRN) 2017 Family Conference in Snowbird, Utah, on Saturday, July 15.

"Treatment with cysteamine bitartrate may cause an unpleasant odor, particularly affecting the patient's breath, and can impact their willingness to maintain continuous cystine-depleting therapy," said Larry Greenbaum, M.D., Ph.D., division director, Department of Pediatric Nephrology, Emory University School of Medicine, who served as principal investigator for the study. "This study is important because people living with nephropathic cystinosis need to be treated with cystine-depleting therapy early and continuously to avoid the serious and potentially life-threatening impact of the disease on tissues and organs."

Summary of Study Results:

- This was an optional substudy of an ongoing Phase 3b long-term open-label study of the safety, tolerability and effectiveness of PROCYSBI versus immediate-release cysteamine. The substudy evaluated 20 patients experiencing halitosis as a side effect while receiving immediate-release cysteamine during the long-term open-label study.
- Patients in the substudy received immediate-release cysteamine for three months, followed by a one-month dose adjustment period before transitioning to PROCYSBI for an additional three months.
- The study compared exhaled dimethyl sulphide concentration in patients treated with immediate-release cysteamine every six hours to levels when treated with PROCYSBI every 12 hours.
- Patients taking PROCYSBI had a 26 percent reduction in exhaled dimethyl sulphide compared with patients taking immediate-release cysteamine.

Most frequently reported adverse events seen in ≥5 percent of patients taking PROCYSBI were vomiting, nausea, abdominal pain, breath odor, diarrhea, skin odor, fatigue and rash.

"We are very pleased to support the Cystinosis Research Network's Family Conference, as these events provide an understanding of the many different challenges faced by people living with nephropathic cystinosis," said Jeffrey W. Sherman, M.D., FACP, executive vice president, research and development and chief medical officer, Horizon Pharma plc. "This halitosis substudy is part of our ongoing effort to analyze the effects of PROCYSBI, because there are many considerations - such as the effect of a medicine on body odor and breath - that are very important for people working to manage their condition while living as normal a life as possible."

In addition to the halitosis substudy (*Quantification of Dimethyl Sulphide Associated with Cysteamine Bitartrate-Induced Halitosis Using Breath Analysis in Cystinosis Patients Treated with Delayed-Release and Immediate-Release Cysteamine Bitartrate*), the following encore presentations, which were presented at previous medical meetings, will be available for viewing at CRN:

- **Title:** *A Pragmatic Trial of Delayed-Release Cysteamine Bitratrate in Children < 6 Years Old with Cystinosis*
  Lead Author: Craig B. Langman, M.D., Feinberg School of Medicine, Northwestern University

- **Title:** *Delayed-Release Cysteamine in Nephropathic Cystinosis Patients after Renal Transplant: A Subgroup Analysis*
  Lead Author: Paul Grimm, M.D., Stanford University School of Medicine

- **Title:** *The Effect of Food and Liquid pH on the Integrity of Enteric-Coated Beads from Cysteamine Bitartrate Delayed-Release Capsules*
  Lead Author: Nadine Pavloff, Ph.D., Horizon Pharma plc

About Cystinosis
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. Elevated cystine 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 cystinosis. Nephropathic or "classic infantile" cystinosis - the most common and most severe form of the disease - is typically diagnosed in infancy and requires lifelong therapy.[1]

About PROCYSBI
In the United States, PROCYSBI® (cysteamine bitartrate) delayed-release capsules is a cystine depleting agent indicated for the treatment of nephropathic cystinosis in adults and pediatric patients two years of age and older.

Important Safety Information

CONTRAINDICATIONS:

- Hypersensitivity to penicillamine or cysteamine.

WARNINGS AND PRECAUTIONS:

- 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.
  • Monitor patients for development of skin or bone lesions and interrupt PROCYSBI dosing if patients develop these lesions. PROCYSBI may be restarted at a lower dose under close supervision, then slowly increase 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, permanently discontinue use of PROCYSBI.
- 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, consider decreasing the dose of PROCYSBI.
- 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.
  • Carefully evaluate and monitor patients who develop CNS symptoms. Interrupt medication or adjust the dose as necessary for patients with severe symptoms or with symptoms that persist or progress.
  • Inform patients that PROCYSBI may impair their ability 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. Monitor white blood cell counts and alkaline phosphatase levels. If tests 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.
  • Monitor patients 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, interrupt dosing or decrease the dose and refer the patient to an ophthalmologist. If the diagnosis is confirmed, permanently discontinue use of PROCYSBI.

ADVERSE REACTIONS:

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.

DRUG INTERACTIONS:

- Drugs that Increase Gastric pH: Administer PROCYSBI at least one hour before or one 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.

USE IN SPECIFIC POPULATIONS:

Lactation: Breastfeeding is not recommended while taking PROCYSBI.

Please see the Full Prescribing Information at www.PROCYSBI.com.

To report SUSPECTED ADVERSE REACTIONS, contact Horizon Pharma at 1-866-479-6742 (Option 1) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

About 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. Follow @HZNPplc on Twitter or view careers on our LinkedIn page.

Forward-Looking Statements
This press release contains forward-looking statements, including statements regarding the potential of PROCYSBI to treat patients with nephropathic cystinosis and the side effects of PROCYSBI. 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 future PROCYSBI results will be in line with prior PROCYSBI results and whether patients are willing to use PROCYSBI to treat nephropathic cystinosis, 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.

References:

1. Cystinosis Research Foundation. "About cystinosis." Available at http://www.cystinosisresearch.org/About-Cystinosis/. Accessed July 12, 2017.

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