Horizon Therapeutics plc Announces U.S. FDA Acceptance of its New Drug Application to Make PROCYSBI® (Cysteamine Bitartrate) Available as Oral Granules in Packets

July 18, 2019

DUBLIN--(BUSINESS WIRE)--Jul. 18, 2019-- Horizon Therapeutics plc (Nasdaq: HZNP) announced today that the U.S. Food and Drug Administration (FDA) has accepted Horizon's New Drug Application (NDA) for PROCYSBI® (Cysteamine Bitartrate) Delayed-Release Oral Granules in Packets. If approved by the FDA, this new dosage form would provide another option for patients, in addition to the currently available PROCYSBI delayed-release capsules. The capsules are FDA-approved for children one year of age and older and adults living with nephropathic cystinosis. The FDA is expected to make a decision on the approval of the proposed new dosage form of granules in packets in 2020.

The proposed new dosage form would provide patients and their caregivers with the option of opening a packet containing small, compact granules and sprinkling on certain foods and juice (or administering through a feeding tube). If approved, these packets would provide an alternative to the currently available option of opening individual capsules to remove the granules.

"A major part of our approach at Horizon is to engage with the cystinosis community throughout the year where we listen, learn and find ways to help," said Gregg Checani, M.D., executive medical director, medical affairs and clinical science, Horizon. "The submission of this NDA is the result of feedback we've received from people living with cystinosis, their caregivers and healthcare professionals, and is part of our ongoing reinvestment into the cystinosis community."

About Nephropathic 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.[1]

About PROCYSBI

INDICATIONS AND USAGE

PROCYSBI (cysteamine bitartrate) delayed-release capsules is a cystine-depleting agent indicated for the treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Patients with serious hypersensitivity reaction, including anaphylaxis 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. Monitor patients for development of skin or bone lesions and reduce PROCYSBI dosing if patients develop these lesions.
- **Skin Rash:** Severe skin rashes such as erythema multiforme bullosa or toxic epidermal necrolysis have been reported in patients receiving immediate-release cysteamine bitartrate. Discontinue use if severe skin rash occurs.
- **Gastrointestinal (GI) Ulcers and Bleeding:** GI ulceration and bleeding have been reported in patients receiving immediate-release cysteamine bitartrate. Monitor for GI symptoms and consider decreasing the dose if severe symptoms occur.
- **Central Nervous System (CNS) Symptoms:** CNS symptoms such as seizures, lethargy, somnolence, depression, and encephalopathy have been associated with immediate-release cysteamine. Monitor for CNS symptoms; interrupt or reduce the dose for severe symptoms or those that persist or progress.
- **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; decrease or discontinue the dose 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 for signs and symptoms of PTC; interrupt or reduce the dose for signs/symptoms that persist, or discontinue if diagnosis is confirmed.

ADVERSE REACTIONS

The most common adverse reactions reported in PROCYSBI clinical trials *(≥ 5%)* were:

- *Patients 2 years of age and older previously treated with cysteamine:* vomiting, nausea, abdominal pain, headache, conjunctivitis, influenza, gastroenteritis, nasopharyngitis, dehydration, ear infection, upper respiratory tract infection, fatigue, arthralgia, cough, and pain in extremity.
- *Patients 1 year of age and older naïve to cysteamine treatment:* vomiting, gastroenteritis/viral gastroenteritis, diarrhea, breath odor, nausea, electrolyte imbalance, headache.

DRUG INTERACTIONS

- Drugs that increase gastric pHmay alter the pharmacokinetics of cysteamine due to the premature release of cysteamine from PROCYSBI and increase WBC cystine concentration. Monitor WBC cystine concentration with concomitant use.
- 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:* Because of the potential risk for serious adverse reactions in breastfed children from cysteamine, breastfeeding is not recommended during treatment with PROCYSBI.

Please see Full Prescribing Information.

About Horizon

Horizon is focused on researching, developing and commercializing medicines that address critical needs for people impacted by rare and rheumatic diseases. Our pipeline is purposeful: we apply scientific expertise and courage to bring clinically meaningful therapies to patients. We believe science and compassion must work together to transform lives. For more information on how we go to incredible lengths to impact lives, please visit www.horizontherapeutics.com, follow us @HorizonNews on Twitter, like us on Facebook or explore career opportunities on LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the potential benefits and means of administration of PROCYSBI Delayed-Release Oral Granules in Packets, if approved, and the expected timing of the FDA's decision with respect to the NDA. 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 the FDA approves the NDA for PROCYSBI Delayed-Release Oral Granules in Packets, Horizon's ability to successfully market PROCYSBI Delayed-Release Oral Granules in Packets, if approved, the availability of reimbursement and payor coverage, as well as those described in Horizon'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 does not undertake any obligation to update or revise these statements, except as may be required by law.

References

1. https://ghr.nlm.nih.gov/condition/cystinosis. Accessed July 16, 2019.

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