Horizon Therapeutics plc Initiates PROTECT Trial Evaluating KRYSTEXXA® (pegloticase injection) to Improve Management of Uncontrolled Gout for Adults with a Kidney Transplant

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-- Trial to evaluate the effectiveness of KRYSTEXXA to sustain reduced serum uric acid levels for post-kidney transplant adults; a vulnerable population --

DUBLIN--(BUSINESS WIRE)--Oct. 17, 2019-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced it has initiated an open-label clinical trial evaluating the use of KRYSTEXXA® (pegloticase injection) in adults with chronic gout refractory to conventional therapies – also known as uncontrolled gout – who have undergone a kidney transplant to demonstrate that KRYSTEXXA may provide effective disease control without burdening the kidneys.

PRO*spective s****T****udy of p****E****gloti****C****ase in* ***T****ransplant patients (PROTECT)* is a multicenter, open-label study which will evaluate the efficacy and safety of KRYSTEXXA among 20 adults with uncontrolled gout who have received a kidney transplant at 15 centers across the U.S. The study and its protocol were thoughtfully designed in collaboration with the American Association of Kidney Patients to incorporate considerations for high-needs populations and their priorities in effectively managing uncontrolled gout.

“The prevalence of gout is more than ten-fold greater among patients who have undergone a kidney transplant than the general population,” said Abdul Abdellatif, M.D. F.A.S.N. primary investigator and assistant professor, Baylor College of Medicine. “Post-transplant medications to prevent organ rejection can also contribute to increased uric acid levels and lead to higher rates of uncontrolled gout. It is here where we have seen higher mortality rates compared to patients who have received a kidney transplant without uncontrolled gout. Strategies to effectively manage uncontrolled gout within the vulnerable post-transplant population are important to ensuring long-term protection of the kidney.”

During the study, participants will receive KRYSTEXXA 8 mg IV every two weeks over a six-month treatment period, with a 3-month post treatment follow-up. The study’s primary endpoint is response rate, as measured by sustained serum uric acid reduction to <6 mg/dL at Month 6 of treatment. It will also evaluate secondary outcomes such as complete resolution of at least one tophus, and scores related to pain and disability. This population was not originally studied in the KRYSTEXXA pivotal trials.

“The unique mechanism of action of KRYSTEXXA provides an opportunity for clinicians to address elevated uric acid levels irrespective of kidney function,” said Paul Peloso, M.D., M.Sc., vice president and therapeutic area head, rheumatology, Horizon. “Working together with our colleagues in the nephrology and transplant communities we designed the PROTECT trial to demonstrate that clinicians can safely and effectively manage uncontrolled gout for individuals who have undergone kidney transplantation.”

More information on the trial can be found on clinicaltrials.gov (NCT04087720).

About Uncontrolled Gout

Gout is a chronic, progressive inflammatory form of arthritis that is caused by excess uric acid in the body and needs to be managed aggressively.[1] Over time uric acid can build up and form deposits, called tophi, inside the body and joints, which can have harmful effects including causing damage to the underlying bone.[2] Patients with uncontrolled gout continue to have abnormally high levels of uric acid and continued symptoms of gout despite the use of conventional therapies. KRYSTEXXA is the only biologic approved by the U.S. Food and Drug Administration (FDA) for the treatment of uncontrolled gout in adult patients.

About KRYSTEXXA

INDICATIONS AND USAGE

KRYSTEXXA® (pegloticase injection) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

Important Limitations of Use: KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

IMPORTANT SAFETY INFORMATION
WARNING: ANAPHYLAXIS AND INFUSION REACTIONS

Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA. Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. However, delayed-type hypersensitivity reactions have also been reported. KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions. Patients should be premedicated with antihistamines and corticosteroids. Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA. Serum uric acid levels should be

monitored prior to infusions, and healthcare providers should consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.

The risk of anaphylaxis and infusion reactions is higher in patients who have lost therapeutic response.

Concomitant use of KRYSTEXXA and oral urate-lowering agents may blunt the rise of sUA levels. Patients should discontinue oral urate-lowering agents and not institute therapy with oral urate-lowering agents while taking KRYSTEXXA.

In the event of anaphylaxis or infusion reaction, the infusion should be slowed, or stopped and restarted at a slower rate.

Patients should be informed of the symptoms and signs of anaphylaxis and instructed to seek immediate medical care should anaphylaxis occur after discharge from the healthcare setting.

CONTRAINDICATIONS: G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA

Patients should be screened for G6PD deficiency prior to starting KRYSTEXXA. Hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. KRYSTEXXA should not be administered to these patients.

GOUT FLARES

An increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy, including treatment with KRYSTEXXA. If a gout flare occurs during treatment, KRYSTEXXA need not be discontinued. Gout flare prophylaxis with a non-steroidal anti-inflammatory drug (NSAID) or colchicine is recommended starting at least 1 week before initiation of KRYSTEXXA therapy and lasting at least 6 months, unless medically contraindicated or not tolerated.

CONGESTIVE HEART FAILURE

KRYSTEXXA has not been studied in patients with congestive heart failure, but some patients in the clinical trials experienced exacerbation. Caution should be exercised when using KRYSTEXXA in patients who have congestive heart failure, and patients should be monitored closely following infusion.

ADVERSE REACTIONS

The most commonly reported adverse reactions in clinical trials with KRYSTEXXA were gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis and vomiting.

Please see Full Prescribing Information and Medication Guide for more 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 of KRYSTEXXA in treating uncontrolled gout in kidney transplant patients and expectations regarding the PROTECT clinical trial. These forward-looking statements are based on management's 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, but are not limited to, risks regarding whether results of the PROTECT trial will be consistent with results of prior trials or Horizon's expectations, and the risks associated with clinical development of drug candidates. For a further description of these and other risks facing Horizon, please see the risk factors 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 undertakes no obligation to update or revise these statements, except as may be required by law.

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[1] Keuhn B. Chronic Disease Approaches Needed to Curb Gout's Growing Burden. Journal of the American Medical Association. 2018;319(13):1308-1309.

[2] Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007-2008. Arthritis Rheum. 2011;63(10):3136-3141.

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