Results from PROTECT Trial Evaluating KRYSTEXXA® (pegloticase injection) in Kidney Transplant Recipients with Uncontrolled Gout Presented as Part of American Society of Nephrology (ASN) Kidney Week

November 4, 2021

-- Complete data from PROTECT trial shows 89% of patients achieved the primary endpoint --

-- Additional presentations call attention to the high prevalence of gout and its associated comorbidities among individuals undergoing dialysis --

DUBLIN--(BUSINESS WIRE)--Nov. 4, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced the presentation of results from the completed PROTECT trial evaluating KRYSTEXXA® (pegloticase injection) in people with chronic gout refractory to conventional therapies, also known as uncontrolled gout, who had received a kidney transplant. In additional presentations, the company shared new insights on the challenges of gout among individuals with chronic kidney disease who undergo dialysis. These data are presented as part of the American Society of Nephrology (ASN) Kidney Week, Nov. 4-7, 2021.

Key KRYSTEXXA presentations include:

Pegloticase for Uncontrolled Gout in Kidney Transplant Recipients: Provisional Data Report of a Multicenter, Open-Label, Efficacy and Safety Study. The results from the completed PROTECT trial (NCT04087720) demonstrated that KRYSTEXXA provided a substantial and sustained decrease in serum uric acid (sUA) for patients with uncontrolled gout who had received a kidney transplant and were treated with two to three immunosuppressive agents to prevent organ rejection. Twenty patients were enrolled in the PROTECT trial. Analysis was conducted based on 18 of 20 patients who did not have a lapse or cessation in treatment due to COVID-19 prior to the Month 6 analysis time-point. Sixteen of 18 patients (88.9%) achieved the primary endpoint, defined as sUA <6 mg/dL for at least 80% of the time during Month 6. In total, six patients discontinued the treatment early, two based on meeting monitoring rules (pre-dose sUA >6 mg/dL at two consecutive visits), three based on COVID-19 pandemic concerns (one included in primary analysis, and two excluded from the primary analysis), and one based on personal reasons not related to adverse events.

At Week 24, health assessment scores for pain and disability improved by 35.5 (baseline: 42.2) and 0.3 (baseline: 1.0), respectively, among those who completed 24 weeks of treatment. Seven serious adverse events reported in five patients were deemed unrelated to treatment, and no anaphylaxis or infusion reaction events occurred.

“Evidence indicates gout is more common, and often more severe, among those who have undergone kidney transplantation, with some data showing a gout prevalence more than 10-fold higher than among non-transplant patients,” said Theresa Podrebarac, M.D., MSc., senior vice president, clinical development, Horizon. “These results indicate KRYSTEXXA can help address uncontrolled gout for one of the most vulnerable populations.”

Please see below for Important Safety Information.

Key gout presentations include:

Risk Factors and Outcomes of Gout in Dialysis Patients: A Cohort Study of the United States Renal Data System (USRDS). A recent review of the 2017 U.S. Renal Data System (USRDS) highlighted new insights on risk factors and outcomes associated with gout among dialysis patients. The study identified more than 41,000 dialysis patients with gout following initiation of chronic outpatient dialysis and compared baseline characteristics, comorbid conditions and clinical outcomes to those without gout. The review found a high prevalence of gout among Medicare patients on dialysis (15%). In all, gout patients were more likely to have a higher prevalence of diabetes, hypertension and cardiovascular conditions (such as heart failure, acute myocardial infarction, ischemic heart disease and stroke) than those without gout. Importantly, the risks of hospitalization and mortality were 11% in the year after index claim.

Characterization of Gout in U.S. Patients Treated with Hemodialysis (HD) and Peritoneal Dialysis (PD). A separate evaluation sought to understand the impact of gout for people undergoing hemodialysis (HD) and peritoneal dialysis (PD) by reviewing patterns of 70,297 HD patients and 5,117 PD patients from the Dialysis and Peritoneal Dialysis Outcomes and Practice Patterns Studies (DOPPS and PDOPPS) for outcomes such as erythropoietin resistance index (ERI), mortality and hospitalization, and patient-reported outcomes (PROs). Gout was found to be common in HD and PD patients (13% prevalence in HD patients and 21% in PD patients). Both HD and PD patients with gout, compared to those without, had a higher prevalence of cardiovascular comorbidities. These comorbidities are a leading cause of mortality in the dialysis patient population.[1,2]

“One-in-four adults with moderate-to-severe CKD are living with gout, creating additional complexities in managing both diseases and contributing additive burden that impacts functional abilities,” said Richard J. Johnson, M.D., professor, Division of Renal Diseases and Hypertension, University of Colorado Denver - Anschutz Medical Campus. “Better understanding the relationship between gout, kidney disease and dialysis offers research opportunities to improve care for patients with gout, particularly to mitigate potentially fatal comorbid conditions such as cardiovascular disease.”

Additional presentations supported by Horizon during ASN Kidney Week include:

- *Claims-Based Evaluation of Pegloticase Use in Gout Patients with a History of Kidney Transplant [PUB317]*

- *Safety of Pegloticase with Immunomodulation Co-Therapy: Literature Review [PUB318]*
- *Baseline Renal Characteristics and Trial Design for MIRROR RCT, Randomized Trial of Pegloticase with or without Methotrexate for Uncontrolled Gout [PUB314]*
- *Gout in Advanced CKD Patients: Prevalence and Impact on Patient Health [PUB316]*

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 the discovery, development and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory 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 and follow us on Twitter, LinkedIn, Instagram and Facebook.

Forward-Looking Statements
This press release contains forward-looking statements, including statements regarding the potential benefits of KRYSTEXXA in treating uncontrolled gout in patients that have received a kidney transplant. 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 additional data from clinical trials or other analyses will be consistent with prior data or Horizon's expectations. 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.

References

1. Fox CS, Matsushita K, Woodward M, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. *Lancet*. 2012;380(9854):1662-1673. doi:10.1016/S0140-6736(12)61350-6.
2. Mahmoodi BK, Matsushita K, Woodward M, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without hypertension: a meta-analysis. *Lancet*. 2012;380(9854):1649-1661. doi:10.1016/S0140-6736(12)61272-0.

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