New Data Evaluating KRYSTEXXA® (pegloticase injection) With Concomitant Immunomodulation to Be Presented at the American College of Rheumatology Convergence 2020

October 8, 2020

-- Presentations will add to the growing body of evidence on the use of KRYSTEXXA with an immunomodulator to impact patient outcomes --

-- Oral presentation on Nov. 7 at 5:20 p.m. ET discussing data from RECIPE, the randomized controlled trial studying the concomitant use of KRYSTEXXA with the immunomodulator mycophenolate mofetil --

-- Horizon to host an online discussion with co-primary investigator for RECIPE on Nov. 10 at 7 p.m. ET --

DUBLIN--(BUSINESS WIRE)--Oct. 8, 2020-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced that data from the investigator-initiated trial, ***RE**du**C**ing **I**mmunogenicity to **P**egloticas**E** (RECIPE),* will be presented during ACR Convergence Nov. 5-9, 2020. Additional studies on the concomitant use of KRYSTEXXA (pegloticase injection) with an immunomodulator to optimize the treatment for people living with chronic gout refractory to conventional therapies (also known as uncontrolled gout) will also be presented.

"In partnership with clinicians, we continue to present real-world experiences in uncontrolled gout and highlight the latest imaging research to illustrate the impact of urate deposition throughout the body," said Jeffrey D. Kent, M.D., FACG, FACP, executive vice president, medical affairs and outcomes research, Horizon. "As the urgency to treat uncontrolled gout has become better understood, we've seen a marked change in the approach to treatment. These changes are reflected by the wide array of data being presented at this year's ACR meeting."

Presentations on KRYSTEXXA co-prescribed with an immunomodulator include:

- **Reducing immunogenicity of pegloticase (RECIPE) with concomitant use of mycophenolate mofetil in patients with refractory gout— results of a Phase 2 double blind randomized controlled trial**
  Proof-of-concept Phase 2 trial on the effect of a short-term course of mycophenolate mofetil (MMF) on pegloticase response rates and mitigation of anti-pegloticase antibody production
  - **Abstract:** 0952, K. Saag
  - (Oral presentation) Saturday, Nov. 7, 2020; 5:20- 5:30 p.m. ET
    Investigator-initiated trial

- **A multi-center efficacy and safety study of methotrexate to increase response rates in patients with uncontrolled gout receiving pegloticase (MIRROR): 12-month results of an open-label study**
  12-month data from the ongoing open-label MIRROR study provides additional insight on how the addition of methotrexate impacts the KRYSTEXXA response rate among people with uncontrolled gout
  - **Abstract:** 0677, J. Botson
  - Saturday, Nov. 7, 2020; 9 – 11 a.m. ET

- **Pharmacokinetics of pegloticase and methotrexate polyglutamate(s) in patients with uncontrolled gout receiving pegloticase and co-treatment of methotrexate**
  This analysis reviews the pharmacokinetics and immunogenicity of KRYSTEXXA when combined with methotrexate, adding new insight supporting an immunomodulation approach to advance outcomes
  - **Abstract:** 0683, M. Weinblatt
  - Saturday, Nov. 7, 2020; 9 – 11 a.m. ET

- **Trends in immunomodulation / pegloticase co-therapy from 2015-2019: A claims database study**
  A new evaluation of claims databases illustrates how immunomodulation approaches with KRYSTEXXA to address uncontrolled gout have been adopted in clinical practice in recent years
  - **Abstract:** 0665, J. Boston
  - Saturday, Nov. 7, 2020; 9 – 11 a.m. ET

- **The impact of azathioprine on the frequency of persistent responsiveness to pegloticase in patients with chronic refractory gout**
  Open label multicenter study to determine whether co-therapy with azathioprine would increase the frequency of chronic refractory gout patients who had persistent urate lowering from pegloticase therapy
  - **Abstract:** 0685, P. Lipsky

- Saturday, Nov. 7, 2020; 9 – 11 a.m. ET
  Investigator-initiated trial

- **Management of gout with pegloticase; real-world utilization and outcomes from TRIO health and the American Rheumatology Network (ARN)**
  Retrospective study on gout-diagnosed patients who initiated their last pegloticase course between July 2015 and Oct. 2019 to identify variables associated with longer time on therapy
  - **Abstract:** 1629, N. Solomon
  - Monday, Nov. 9, 2020; 9 – 11 a.m. ET
    Independent study

In addition, Horizon will host an online discussion on Nov. 10 at 7 p.m. ET about KRYSTEXXA and immunomodulation, featuring Puja Khanna, M.D., M.P.H., co-primary investigator for RECIPE, and moderated by Brian LaMoreaux, M.D., M.S., Horizon medical director.

The safety and efficacy of KRYSTEXXA concomitantly used with an immunomodulator has not been established by any health authorities.

Please see important safety information for KRYSTEXXA below.

Presentations on risk factors and systemic impact associated with gout include:

- **Dual Energy CT Has Additional Prognostic Value Over Clinical Measures in Gout Including Tophi: A Best Evidence Synthesis**
  Best evidence synthesis framework summary of the evidence for Dual Energy CT Scan (DECT) as a prognostic gout tool
  - **Abstract:** 0648, S. Stauder
  - Saturday, Nov. 7, 2020; 9 – 11 a.m. ET

- **Gout and Serum Urate Levels are Associated with Lumbar Spine Monosodium Urate Deposition and Chronic Low Back Pain: A Dual-Energy CT Study**
  Prospective study using dual-energy CT (DECT) to determine the prevalence and extent of monosodium urate deposition in the lumbosacral spines of patients with gout vs without gout, and with tophaceous vs non-tophaceous gout
  - **Abstract:** 0681, M. Pillinger
  - Saturday, Nov. 7, 2020; 9 – 11 a.m. ET
    Investigator-initiated trial

- **Cause-Specific Mortality in Patients with Gout in the Veteran's Health Administration: A Matched Cohort Study**
  Retrospective, matched cohort study, to compare all-cause and cause-specific mortality risk between gout and non-gout patients in the VHA between Jan. 1999 to Sept. 2015
  - **Abstract:** 0662, T. Mikuls
  - Saturday, Nov. 7, 2020; 9 – 11 a.m. ET
    Investigator-initiated trial

- **Change in Tophus Size Measured with Dual-energy CT and Ultrasound: A 1-year Multicenter Follow-up Study**
  Study of the evolution of tophus volume measured with dual energy CT scans and ultrasounds to determine coloration during the first year of urate lowering therapy
  - **Abstract:** 1550, T. Pascart
  - Monday, Nov. 9, 2020; 9 – 11 a.m. ET
    Investigator-initiated trial

- **Gout and Heart Failure in the U.S.**
  Review of the Nationwide Inpatient Sample (NIS) database on the clinical and economic consequences of gout and hyperuricemia as significant risk factors for heart failure
  - **Abstract:** 0657, G. Singh
  - Saturday, Nov. 7, 2020; 9 – 11 a.m. ET
    Investigator-initiated trial

- **Gout is an Independent Risk Factor for Undergoing an Amputation Procedure**
  A U.S. claims database review to examine the occurrence of amputations (foot, toes, hand, fingers) in adult patients with gout and in those with diabetes
  - **Abstract:** 0673, S. Neville
  - Saturday, Nov. 7, 2020; 9 – 11 a.m. ET

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 and follow us on Twitter, LinkedIn, Instagram and Facebook.

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