Horizon Pharma plc Initiates Clinical Trial to Evaluate KRYSTEXXA® (pegloticase injection) with Methotrexate to Enhance Response Rates for People Living with Uncontrolled Gout

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DUBLIN--(BUSINESS WIRE)--Sep. 27, 2018-- Horizon Pharma plc (Nasdaq: HZNP) enrolled the first patient in a clinical trial evaluating the use of KRYSTEXXA® (pegloticase injection) with methotrexate to sustain lower serum uric acid (sUA) levels of people living with chronic gout refractory to conventional therapies – also known as uncontrolled gout – and increase persistence of efficacy on therapy. The clinical trial, ***M**ethotrexate to **I**ncrease **R**esponse **R**ates in Patients With Uncontrolled G**O**ut **R**eceiving KRYSTEXXA (MIRROR),* will enroll approximately 30 patients and is an adaptive design study to evaluate the use of methotrexate as an immunomodulator to meaningfully attenuate an immune response to KRYSTEXXA in adults living with uncontrolled gout.

"In the pivotal clinical trials evaluating KRYSTEXXA 42 percent of patients achieved complete response, maintaining a serum uric acid level of less than six mg/dL over six months," said Jeff R. Peterson, M.D., president, Washington Rheumatology Alliance and a director at Northwest Rheumatism Society and Western Washington Medical Group Arthritis Clinic's clinical research department. "Many biologics have an improved response rate when they are co-prescribed with methotrexate, which works to reduce anti-drug antibodies. It is through research that we gain valuable insights for KRYSTEXXA, an important therapy for patients with progressive signs and symptoms of gout despite the use of oral therapies."

“For patients with uncontrolled gout, it is imperative to rapidly reduce serum uric acid level levels in order to address the disease and its effect on joints, tissues and organ systems,” said John K. Botson M.D., R.Ph., C.C.D., president, Alaska Rheumatology Alliance and rheumatologist, Orthopedic Physicians Alaska. “Methotrexate is very familiar to rheumatologists, and it may allow more patients on KRYSTEXXA to continue over the treatment period.”

Those who meet MIRROR (NCT03635957) eligibility criteria will receive methotrexate 15 mg orally once weekly starting four weeks before and continued through 24 weeks of bi-weekly infusions of KRYSTEXXA. The primary endpoint will be sUA responder rate which is defined as maintaining an sUA level of < 6 mg/dL for at least 80 percent of the time during weeks 10, 12 and 14, as well as having at least one sUA level <5 mg/dL between the first KRYSTEXXA infusion and through week 14. In addition, MIRROR will assess several secondary endpoints including sUA responder rate at weeks 20, 22, and 24 as well as proportion of overall sUA responders at weeks 10, 12, 14, 20, 22, and 24 combined.

“Real-world feedback from the medical community informed our selection of methotrexate as the immunomodulator in this study,” said Paul Peloso, M.D., M.Sc., vice president and therapeutic area head, rheumatology, Horizon Pharma plc. “MIRROR complements two ongoing investigator-initiated trials of KRYSTEXXA with other commonly used immunomodulators, azathioprine and mycophenolate mofetil. This trial is part of our comprehensive clinical strategy to address the burden of uncontrolled gout.”

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] 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. For more information, please visit www.KRYSTEXXAHCP.com.

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 patients 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.

Forward Looking Statements

This press release contains forward-looking statements, including statements regarding the potential benefits of combining methotrexate treatment with KRYSTEXXA and expectations regarding the MIRROR clinical trial. 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. 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 MIRROR trial will be consistent with results of prior trials or Horizon Pharma'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 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 undertakes no obligation to update or revise these statements, except as may be required by law.

About Horizon Pharma plc

Horizon Pharma plc is focused on researching, developing and commercializing innovative medicines that address unmet treatment needs for rare and rheumatic diseases. By fostering a growing pipeline of medicines in development and exploring all potential uses for currently marketed medicines, we strive to make a powerful difference for patients, their caregivers and physicians. For us, it's personal: by living up to our own potential, we are helping others live up to theirs. For more information, please visit www.horizonpharma.com, follow us @HZNPplc on Twitter, like us on Facebook or explore career opportunities on LinkedIn.

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