Horizon Therapeutics plc Initiates Clinical Trial to Assess Shorter Infusion Duration for KRYSTEXXA® (pegloticase injection) Concomitantly Used with Methotrexate to Treat Uncontrolled Gout

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-- The AGILE trial is designed based on patient and clinician input and part of Horizon's continued investment to impact the KRYSTEXXA patient experience --

DUBLIN--(BUSINESS WIRE)--Oct. 29, 2020-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced that the first patient has been enrolled in the *Infusion Duration Study to Assess Tolerability of Pegloticase Administered with a Shorter Infusion Duration in Subjects with Uncontrolled Gout Receiving Methotrexate*, or AGILE, clinical trial to evaluate a shorter infusion duration for KRYSTEXXA® (pegloticase injection) co-prescribed with methotrexate to treat people with chronic gout refractory to conventional therapies, also known as uncontrolled gout.

Biologic therapies, like KRYSTEXXA, are often administered through infusions that deliver the therapeutic into the body over a period of time. Currently, KRYSTEXXA is infused for at least two hours. Based on input from the patient community, Horizon has designed this Phase 4, multicenter, open-label study to assess the safety and efficacy of KRYSTEXXA co-prescribed with methotrexate when administered over a shorter period of time.

"As clinicians, we understand the urgency to treat uncontrolled gout and address its effects 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. "A shorter infusion duration for KRYSTEXXA could meaningfully impact the experience for patients, clinicians and sites of care."

AGILE will enroll from 30 to 50 adult participants with uncontrolled gout.[1] After four weeks of treatment with methotrexate, participants will receive up to 24 weeks of weekly oral methotrexate and biweekly KRYSTEXXA infusions (8 mg) in one of three sequential assigned infusion durations: 60-minute infusion, 45-minute infusion and 30-minute infusion. Each study segment will include a minimum of 10 participants. This trial will primarily focus on safety and tolerability of each infusion duration.

This trial initiation follows the recent announcement that data from the *Methotrexate to Increase Response Rates in Patients With Uncontrolled Gout Receiving KRYSTEXXA, or* MIRROR, open-label trial was published in the *Journal of Rheumatology*[2] and that the company's MIRROR randomized controlled trial[3] evaluating the concomitant use of KRYSTEXXA with methotrexate to improve response rates reached target enrollment. The safety and efficacy of KRYSTEXXA co-prescribed with methotrexate has not been established by any health authorities.

"AGILE reflects our efforts to innovate and improve experiences based on the input from patients, their families and clinicians," said Paul Peloso, M.D., M.Sc., vice president and therapeutic area head, rheumatology, Horizon. "Through trials like this and our MIRROR clinical program, Horizon continues to advance understanding of uncontrolled gout and treatment approaches that help to improve patient outcomes."

More information about the trial can be found on clinicaltrials.gov (NCT 04511702).

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.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the potential benefits of a shorter infusion duration of KRYSTEXXA, expectations regarding the AGILE clinical trial, and Horizon's product development strategy and plans. 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 AGILE clinical trial will be consistent with results of prior trials or other data or Horizon's expectations and the risks associated with clinical development. 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. National Institute of Health. Infusion Duration Study To Assess Tolerability of Pegloticase Administered With a Shorter Infusion Duration in Subjects With Uncontrolled Gout Receiving Methotrexate (AGILE). https://clinicaltrials.gov/ct2/show/NCT04511702. Accessed Oct. 16, 2020.
2. Botson JK, Tesser JRP, Bennett R, et al. Pegloticase in combination with methotrexate in patients with uncontrolled gout: A multicenter, open-label study (MIRROR). *J Rheumatol*. 2020 Sep 15:jrheum.200460.
3. National Institute of Health. Study of KRYSTEXXA® (pegloticase) plus methotrexate in patients with uncontrolled gout (MIRROR RCT). https://www.clinicaltrials.gov/ct2/show/NCT03994731. Accessed October 26, 2020.

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