RECIPE Randomized Controlled Trial Data Published in Arthritis & Rheumatology Show Higher Response Rates Using KRYSTEXXA® (pegloticase injection) with the Immunomodulator Mycophenolate Mofetil

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-- Primary study endpoint demonstrates 86 percent response rate for patients receiving co-therapy of KRYSTEXXA and mycophenolate mofetil --

DUBLIN--(BUSINESS WIRE)--Apr. 7, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) announced the publication of data from the first randomized controlled clinical trial (RCT) of KRYSTEXXA (pegloticase injection) concomitantly used with an immunomodulator, mycophenolate mofetil, in *Arthritis & Rheumatology* [doi.org/10.1002/art.41731].

The Reducing Immunogenicity of Pegloticase (RECIPE) trial demonstrated that 86 percent of patients (19 of 22) receiving co-therapy of KRYSTEXXA with the immunomodulator mycophenolate mofetil achieved serum uric acid (sUA) ≤ 6 mg/dL at 12 weeks, the primary study endpoint, compared to 40 percent of patients (4 of 10) receiving KRYSTEXXA monotherapy. The safety and efficacy of KRYSTEXXA co-prescribed with mycophenolate mofetil has not been established by any health authorities.

“Our focus on urgently reducing the buildup of uric acid crystals and addressing the impact of uncontrolled gout on patients led us to explore how to curtail the development of anti-drug antibodies with pegloticase through the RECIPE trial,” said Puja Khanna, M.D., M.P.H., associate professor and rheumatologist at the University of Michigan, and co-primary investigator for the RECIPE trial. “This trial adds major insight to the evolving body of data – that co-treatment with immunomodulatory medications can mitigate antibody production, and thereby improve the response rates of pegloticase. We believe that this novel approach has the potential of meaningfully improving the patient’s response to urate lowering therapy and long-term outcomes as a result.”

Data from this investigator-initiated Phase 2, double-blind, placebo-controlled proof-of-concept trial led by the University of Alabama at Birmingham and University of Michigan funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and Horizon illustrate the effect of a concomitant regimen of KRYSTEXXA with mycophenolate mofetil. In the study, 35 adult patients with uncontrolled gout were randomized (3:1) to receive either mycophenolate mofetil or placebo for two weeks prior to starting KRYSTEXXA (12 infusions of 8 mg every two weeks). Thirty-two patients received at least one dose of KRYSTEXXA and were included in the analysis, with three patients discontinuing prior to the first KRYSTEXXA infusion. During the trial, patients continued to receive either mycophenolate mofetil (1g) twice daily or placebo with KRYSTEXXA for 12 weeks. After Week 12, all patients received only KRYSTEXXA 8 mg IV every two weeks for 12 weeks, providing six months of KRYSTEXXA therapy. The primary endpoint was the proportion of patients who reached and maintained response to therapy (defined as sUA levels ≤6 mg/dL at 12 weeks).[1]

In total, 86 percent (19 of 22) of patients receiving co-therapy of KRYSTEXXA and mycophenolate mofetil achieved serum uric acid ≤ 6 mg/dL at Week 12 versus 40 percent (4 of 10) of patients in the KRYSTEXXA and placebo arm, with a sustained response at Week 24 in 68 percent (15 of 22) of patients versus 30 percent (3 of 10) of patients, respectively. In the KRYSTEXXA with mycophenolate mofetil arm, no (0 of 22 patients) infusion reactions were reported compared to 30 percent (3 of 10) of patients reporting infusion reactions in the KRYSTEXXA with placebo arm. The most commonly reported adverse events for the KRYSTEXXA with mycophenolate mofetil arm versus the KRYSTEXXA with placebo arm included musculoskeletal (41 percent versus 10 percent), gastrointestinal disorders (18 percent versus 10 percent), respiratory (18 percent versus 0 percent) and infections (9 percent versus 0 percent).[1]

“This publication reflects a fundamental aspect of our collaborative research efforts with leading voices in the rheumatology community,” said Paul M. Peloso, M.D., M.Sc., vice president and therapeutic area head, rheumatology, Horizon. “As we listen to and learn from studies outside of Horizon, along with our clinical colleagues, we can refine strategies to best improve the utility of our medicines and optimize benefits to 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 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 combining immunomodulator (including mycophenolate mofetil) treatment with KRYSTEXXA. 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 additional clinical trials will be consistent with results of prior trials or other data or Horizon's expectations, the risks associated with clinical development of drug candidates and risks related to competition or other factors that may change physician treatment strategies. 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. Khanna, P, et al. Reducing Immunogenicity of Pegloticase (RECIPE) with Concomitant Use of Mycophenolate Mofetil in Patients with Refractory Gout — a Phase II Double Blind Placebo Controlled Randomized Trial *Arthritis & Rheumatology*. 2021. doi:10.1002/art.41731

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