Horizon Therapeutics plc Submits Supplemental Biologics License for the Concomitant Use of KRYSTEXXA® (pegloticase injection) Plus Methotrexate for People Living with Uncontrolled Gout

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-- Submission based on recent results from the MIRROR randomized clinical trial, which showed a 71% response rate for patients randomized to receive KRYSTEXXA plus methotrexate --

DUBLIN--(BUSINESS WIRE)--Jan. 10, 2022-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced that it has submitted a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) to expand the approved indication for KRYSTEXXA plus methotrexate, an immunomodulator commonly prescribed by rheumatologists.

"Horizon has invested substantially in research and development efforts to improve the safety and efficacy of KRYSTEXXA in the various patient populations who are affected by uncontrolled gout," said Theresa Podrebarac, M.D., M.Sc., senior vice president, clinical development, Horizon. "We are committed to actively advancing research and addressing the long-term consequences for this often overlooked, stigmatized disease. Since 2018, we have seen a paradigm shift in uncontrolled gout care, which has been reinforced by the positive MIRROR randomized controlled trial results. Today's filing reflects these trends and will help to further evolve the standard of care in uncontrolled gout."

KRYSTEXXA is currently indicated for the treatment of chronic gout refractory to conventional therapies, also known as uncontrolled gout, in adult patients,[1] and has demonstrated rapid reduction in serum uric acid (sUA) for people with uncontrolled gout.[2] As treatment with biologic medicines can, in some people, trigger the body's immune system to develop anti-drug antibodies, immunomodulators such as methotrexate are often used to help improve response rates.[3]

The sBLA submission is based on the Methotrexate to Increase Response Rates in Patients with Uncontrolled Gout Receiving KRYSTEXXA trial (MIRROR randomized controlled trial [RCT]) with supporting evidence from the MIRROR open-label trial, as well as published data from several independent case series showing improved treatment response rates through the use of KRYSTEXXA plus methotrexate.[4-7] The MIRROR randomized controlled trial results, announced in October 2021, showed 71.0% (71 of 100 patients) of patients who were randomized to receive KRYSTEXXA plus methotrexate achieved a complete sUA response, defined as sUA <6 mg/dL at least 80% of the time during Month 6.

Subsequent to the October 2021 announcement, the placebo (monotherapy) response rate was adjusted to 38.5% (20 of 52 patients), as one patient had incorrectly been counted as a responder despite meeting sUA monitoring protocol. The trial demonstrated a 32.5-percentage point improvement for those randomized to receive KRYSTEXXA plus methotrexate compared to those randomized to KRYSTEXXA with placebo ($p<0.0001$).[4] These trial results are aligned with the original pivotal clinical trials of KRYSTEXXA monotherapy, which showed 42% (36 of 85) of dosed patients had a complete sUA response during Months 3 and 6 combined.[8] No new safety concerns were identified.

The sBLA seeks to update the prescribing information to include KRYSTEXXA plus methotrexate to help more patients achieve a complete and durable response to therapy by decreasing the development of anti-drug antibodies. Horizon expects the FDA to complete its review during the second half of 2022.

About KRYSTEXXA

INDICATION 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, 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 co-treatment of KRYSTEXXA with methotrexate for uncontrolled gout, Horizon's research and development plans and strategy and expected timing of the FDA's review of Horizon's sBLA submission. 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 the timing and results of the FDA's review of the sBLA submission, whether additional data from clinical trials or other analyses will be consistent with prior data or Horizon's expectations and risks related to the adoption of co-treatment of KRYSTEXXA with methotrexate for uncontrolled gout. 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

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