Horizon Therapeutics plc Presents New Data on Robust Pipeline at EULAR European Congress of Rheumatology

June 2, 2021

-- Early data from ongoing PROTECT trial suggest stable and durable response to KRYSTEXXA® (pegloticase injection) therapy in treating uncontrolled gout among people with kidney transplants --

-- Data on the company's investigational compound (HZN-4920) under evaluation for rheumatoid arthritis will be presented during an oral session on June 3 at 10:15 a.m. CEST --

DUBLIN--(BUSINESS WIRE)--Jun. 2, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) today presented new data during the EULAR European Congress of Rheumatology from the ongoing PROTECT study, which provides further insight into utility of KRYSTEXXA (pegloticase injection) as a treatment for people with uncontrolled gout (chronic gout refractory to conventional therapies) who have undergone a kidney transplant.

The Prospective Study of Pegloticase in Transplant patients (PROTECT) trial is an ongoing Phase 4, multi-site, open-label trial evaluating the safety and efficacy of KRYSTEXXA in adults with uncontrolled gout who have received a kidney transplant and are on stable immunosuppressive therapy. Participants are receiving KRYSTEXXA (8 mg once every two weeks for 24 weeks) to determine response rate (defined as serum uric acid (sUA) <6 mg/dL for at least 80 percent of the time) during Month 6.[1]

At time of data cut, estimated glomerular filtration rate (eGFR), a key indicator of kidney function, remained stable for all patients throughout KRYSTEXXA treatment. In the 10 patients with Week 24 eGFR measurements, the mean eGFR was 41.6 ± 10.6 mL/min/1.73 m^2 (median of 41.0) at baseline and 43.8 ± 11.9 mL/min/1.73 m^2 (median of 46.6) at Week 24, with a mean improvement of 2.3 ± 8.1 mL/min/1.73 m^2 during the treatment. Further, through health assessment questionnaires, patients reported clinically meaningful reductions in pain (average reduction of 26.7 +/- 30.3 from baseline of 35.9 +/- 30.2 on a scale of 0-100) and disability (average reduction of 0.2 +/- 0.5 from baseline of 1.0 +/- 1.0 on a scale of 0-3).

"Given kidney transplant patients have a 10-fold or higher prevalence of gout compared to non-transplant patients, it is particularly important to effectively manage this disease," said Abdul Abdellatif, M.D. F.A.S.N. primary investigator and adjunct assistant professor, Baylor College of Medicine Nephrology Division, and Kidney Hypertension Transplant Clinic of Clearlake Specialties. "Expanding datasets from the PROTECT trial indicated that KRYSTEXXA could represent a durable and tolerable therapy for this sensitive patient population."

The PROTECT trial was fully enrolled in January 2021 with 20 patients who received a kidney transplant and as such were on two to three immunosuppressive agents each. At the time of data analysis, 10 patients had completed the full course of therapy and five were receiving ongoing treatment; three patients discontinued the study (one withdrew consent, two withdrew due to COVID-19 concerns) and two discontinued treatment due to meeting sUA monitoring protocols. In the trial, 15 patients experienced an adverse event, with the majority (12 of 15 patients) reporting mild-to-moderate events, none of which led to discontinuation of therapy. No anaphylaxis or infusion reaction events were reported. The trial is expected to be completed in Fall 2021. ***Preliminary findings of the PROTECT clinical trial: pegloticase efficacy and safety in kidney transplant recipients (Abstract: POS1122)***

"The persistent challenge of a chronic disease like gout requires that we understand how the experience varies among patient populations, especially more vulnerable populations like kidney transplant recipients, and design regimens accordingly to meet treatment goals," said Jeffrey D. Kent, M.D., FACG, FACP, executive vice president, medical affairs and outcomes research, Horizon. "The data we continue to collect through robust research programs on KRYSTEXXA provides not only clarity on the role of this important therapy, but also confidence to physicians that this can support holistic patient care."

Additional KRYSTEXXA Presentations

Other KRYSTEXXA presentations during EULAR include posters highlighting the pharmacokinetic and anti-drug antibody profile when KRYSTEXXA is co-administered with methotrexate as part of the MIRROR open-label trial ***(Pharmacokinetics of Pegloticase and Methotrexate Polyglutamate(s) in Patients with Uncontrolled Gout Receiving Pegloticase and Co-treatment of Methotrexate [Abstract POS1136])***, as well as real world insights on the demographics, comorbidities and renal functions of people who received KRYSTEXXA ***(Demographics, Comorbidities, and Renal Function of Uncontrolled Gout Patients Who Received Pegloticase: Finding From A Large US Claims Database [Abstract POS1121])***. Notably, data from the U.S. claims database found that 83 percent (40 of 48) of people who had a full course of treatment captured experienced stable or improved chronic kidney disease. For people with advanced chronic kidney disease (Stages 3- 5), data showed that 89 percent (16 of 18 people) experienced stable or improved chronic kidney disease.

Oral Presentation on HZN-4920

Additionally, during an oral session on June 3, 2021 at 10:15 a.m. CEST, the company will present data assessing the duration of clinical improvement beyond Day 169 of its original 2019 trial of people with moderate-to-severe rheumatoid arthritis (RA). This observational follow-up study of 16 out of 24 patients, who had received 1000 mg or 1500 mg HZN-4920 at one of two sites in Poland, showed that HZN-4920 added to stable DMARD therapy may provide a prolonged, clinically meaningful benefit to patients with moderate to severe RA. Duration of clinically meaningful benefit was assessed by need for rescue therapy. Interpretation of these data is limited. The duration of clinical response needs to be confirmed in prospective, double-blind,

placebo-controlled studies. (***Duration of Clinical Efficacy Following Treatment with VIB4920 in Subjects with Moderate to Severe Rheumatoid Arthritis (Abstract: OP0120)***

About HZN4920

This investigational compound is a fusion protein binding CD40L on T cells, blocking their interaction with CD40-expressing B cells. Horizon is currently conducting Phase 2 clinical trials with HZN4920 in **Sjögren's syndrome** , **rheumatoid arthritis** and **kidney transplant rejection**.

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 KRYSTEXXA and HZN-4920 and expectations regarding the PROTECT clinical trial. 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 future results of the PROTECT clinical trial and on-going Phase 2 clinical trials of HZN-4920 will be consistent with preliminary results or 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. National Institutes of Health. Study of Pegloticase in Patients with Uncontrolled Gout Who Have Had a Kidney Transplant. https://clinicaltrials.gov/ct2/show/NCT04087720. Accessed May 25, 2021.

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