June 14, 2017

Horizon Pharma plc Presents New Data Analyses Further Demonstrating Clinical Benefit of KRYSTEXXA® (pegloticase) in Patients with Uncontrolled Gout

Data Show Benefit of KRYSTEXXA Regardless of Clinically Apparent Tophi

DUBLIN, Ireland, June 14, 2017 (GLOBE NEWSWIRE) -- Horizon Pharma plc (NASDAQ:HZNP), a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs, today announced that four new data analyses evaluating the use of KRYSTEXXA® (pegloticase) in patients with refractory chronic gout will be presented at the Annual European Congress of Rheumatology (EULAR) 2017 in Madrid on June 15, 2017.

One study (*Characterization of Patients with Chronic Refractory Gout Who Do and Do Not Have Clinically Apparent Tophi: Response to Pegloticase;* abstract THU0448) retrospectively analyzed data from two pivotal, six-month, randomized clinical trials comparing patients with and without clinically apparent tophi, which are hard uric acid deposits under the skin that contribute to bone and cartilage destruction. In the analysis, both groups showed significant clinical benefit, improvement in tender or swollen joints, quality of life and reduction in flares, over six months of treatment with KRYSTEXXA.

"All gout is tophaceous, but many patients dealing with chronic, painful symptoms may not have visible tophi," said Jeffrey W. Sherman, M.D., FACP, executive vice president, research and development and chief medical officer, Horizon Pharma plc. "This retrospective analysis indicates that KRYSTEXXA provided benefit not only among patients dealing with the challenges typically associated with clinically apparent tophi - such as disability - but also among those who do not have visible tophi."

Summary of Results

- The study compared 62 patients who had clinically apparent tophi at baseline and 23 patients who did not.
- At baseline, patients with clinically apparent tophi had more tender and swollen joints, greater disability, and greater arthritis severity, but otherwise their clinical presentation was similar to patients without clinically apparent tophi.
- Both groups had significant clinical benefit over six months of treatment with KRYSTEXXA.
- Among patients with clinically apparent tophi, at six months of KRYSTEXXA treatment there were significant reductions in serum uric acid ($p < 0.0001$), flares ($p < 0.0001$), Patient Global Assessment (PGA; $p < 0.0001$), tender and swollen joints (TJC and SJC; both $p < 0.0001$), the Health Assessment Questionnaire-Disability Index (HAQ-DI; $p=0.02$) and Bodily Pain from the Medical Outcomes Study Short Form 36 item (SF-36; $p < 0.0001$).
- Among patients without clinically apparent tophi, at six months of KRYSTEXXA treatment there were significant reductions in serum uric acid ($p < 0.0001$), flares ($p=0.003$), PGA ($p=0.009$), TJC ($p=0.01$) and SJC ($p=0.003$), the Arthritis-Specific Health Index (ASHI; $p=0.0001$) and SF-36 ($p=0.03$).
- The most commonly reported adverse reactions in clinical trials with KRYSTEXXA are gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis and vomiting.

"Too many patients endure regular gout flares and get to a point where they simply feel out of options," said Peter E. Lipsky, M.D., director of clinical operations for AMPEL BioSolutions, and author of the study. "These data provide important information for rheumatologists and other healthcare providers about the use of KRYSTEXXA for patients living with the painful and debilitating symptoms of chronic gout, including those with and without visible tophi."

Findings from another retrospective analysis (*Rapid Tophus Resolution in Chronic Refractory Gout Patients Treated with Pegloticase*; abstract THU0416) of data from the same pivotal clinical trials showed that KRYSTEXXA rapidly resolved tophi in patients considered to be responders by profoundly lowering and maintaining serum uric acid levels. Responders were defined as patients who had uric acid levels less than 6.0 mg/dl for 80 percent of the clinical study during extensive monitoring.

KRYSTEXXA is the only medicine approved by the U.S. Food and Drug Administration (FDA) for the treatment of refractory chronic gout, which represents an orphan disease subset of the common form of gout. In general, gout is a type of chronic inflammatory arthritis in which uric acid builds up in the blood and can lead to severe pain and joint destruction. Patients with refractory chronic gout continue to have abnormally high levels of uric acid and continued symptoms despite the use of conventional therapies.

Schedule of Data Analyses Presented at EULAR Congress 2017

- **Title:** *Characterization of Patients with Chronic Refractory Gout Who Do and Do Not Have Clinically Apparent Tophi: Response to Pegloticase*
  Authors: N. L. Edwards, J. Singh, O. Troum, A. Yeo, P. Lipsky
  Date: Thursday, June 15, 2017
  Time: 11:45 CET
  Poster #: THU0448

- **Title:** *Rapid Tophus Resolution in Chronic Refractory Gout Patients Treated with Pegloticase*
  Authors: B. Mandell, A. Yeo, P. Lipsky
  Date: Thursday, June 15, 2017
  Time: 11:45 CET
  Poster #: THU0416

- **Title:** *Evidence Based Development of Criteria for Complete Response in Patients with Chronic Refractory Gout*
  Authors: N. Schlesinger, P. Khanna, A. Yeo, P. Lipsky
  Date: Thursday, June 15, 2017
  Time: 11:45 CET
  Poster #: THU0449

- **Title:** *Lack of Predictive Value of the NIAID/FAAN Criteria to Identify Subjects with Evidence of Immune Activation After Receiving Pegloticase for Chronic Refractory Gout*
  Authors: L. Calabrese, A. Kavanaugh, A. Yeo, P. Lipsky
  Date: Thursday, June 15, 2017
  Time: 11:45 CET
  Poster #: THU0438

About KRYSTEXXA®

INDICATIONS AND USAGE

KRYSTEXXA® (pegloticase) is indicated for the treatment of chronic gout in adult 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

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. Monitor serum uric acid levels prior to infusions and 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.

Inform patients of the symptoms and signs of anaphylaxis, and instruct them to seek immediate medical care should anaphylaxis occur after discharge from the healthcare setting.

CONTRAINDICATIONS: G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA

Screen patients for G6PD deficiency prior to starting KRYSTEXXA. Life threatening hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. Do not administer KRYSTEXXA to patients with G6PD deficiency.

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 formally studied in patients with congestive heart failure, but some patients in the clinical trials experienced exacerbation. Exercise caution when using KRYSTEXXA in patients who have congestive heart failure and monitor patients closely following infusion.

ADVERSE REACTIONS
The most commonly reported adverse reactions in clinical trials with KRYSTEXXA are 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 Pharma plc
Horizon Pharma plc is a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs. The Company markets 11 medicines through its orphan, rheumatology and primary care business units. For more information, please visit www.horizonpharma.com. Follow @HZNPplc on Twitter or view careers on our LinkedIn page.

Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to the benefits of KRYSTEXXA to patients with gout, and other statements that are not historical facts. These forward-looking statements are based on Horizon Pharma's current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward looking statements as a result of these risks and uncertainties, which include, without limitation, risks related to the impact of KRYSTEXXA on patients with gout differing from historical results and healthcare providers not using KRYSTEXXA with gout patients, as well as other risks related to Horizon Pharma's business detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon Pharma's SEC filings and reports, including in its Annual Report on Form 10-K for the year ended December 31, 2016 and subsequent quarterly reports on Form 10-Q. Horizon Pharma undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information, future events or changes in its expectations.

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