



## Horizon Pharma plc Presents New Data at 2017 ACR/ARHP Annual Meeting, Advances Clinical Understanding of KRYSTEXXA® (pegloticase injection) in Adults with Uncontrolled Gout

November 6, 2017

-- Initial data from investigator-initiated TRIPLE study shows infusion reactions occurred in less than 1 percent of infusions --

-- Analyses further support the efficacy and safety of KRYSTEXXA --

DUBLIN, Ireland, Nov. 06, 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 new data evaluating KRYSTEXXA® (pegloticase injection) will be shared in four poster presentations this week at the 2017 ACR/ARHP Annual Meeting, Nov. 3-8, in San Diego. These data include initial results from an investigator-initiated dosing study, as well as three post-hoc analyses of KRYSTEXXA clinical trials, and are part of Horizon Pharma's ongoing efforts to advance the science and ultimately improve outcomes for people living with chronic gout refractory to conventional therapies, also known as uncontrolled gout.

"We've heard many firsthand accounts of the debilitating pain experienced by people living with uncontrolled gout and are driven to further our research and understanding of KRYSTEXXA for those who continue to suffer from agonizing symptoms and associated health problems like high blood pressure or chronic kidney disease," said Jeffrey W. Sherman, M.D., FACP, executive vice president, research and development and chief medical officer, Horizon Pharma plc. "By partnering with the leaders in the scientific community, Horizon Pharma has made significant progress improving the understanding of KRYSTEXXA's safety profile. The TRIPLE study incorporated many of these learnings and the results show that proper utilization of the KRYSTEXXA stopping rules may reduce the risk for infusion reactions."

The initial results from the investigator-initiated TRIPLE (Tolerization Reduces Intolerance to Pegloticase and Prolongs the Urate Lowering Effect) study presented today at ACR/ARHP offer further understanding into factors that influence response and show a notable reduction in the frequency of infusion reactions (IRs). Additionally, data from the three post-hoc analyses of KRYSTEXXA show the connection of lower serum uric acid (sUA) levels to a reduction in blood pressure, a reduction in tophi and an ability for patients to reach complete response (CR).

"TRIPLE is the first study to show prospectively that when treatment 'stopping rules' are used, which is occurring more frequently in real-world practice, the rate of infusion reactions can be meaningfully reduced," said Peter E. Lipsky, M.D., one of the authors of the poster presentation and director of clinical operations for AMPEL BioSolutions. "We saw a remarkable decrease in the frequency of infusion reactions during this study. Further research through TRIPLE and continued evaluation will help to clarify factors that influence response such as tolerization dose, schedule, demographic factors and the utilization of concomitant immunomodulation."

### Data Summaries Presented at ACR/ARHP 2017

#### **Initial Results of a Clinical Study to Determine Whether a Tolerizing Regimen of Pegloticase Can Increase the Frequency of Subjects Having Sustained Lowering of Serum Urate (abstract [1141](#))**

Initial results presented from an ongoing investigator-initiated TRIPLE study show the tolerization regimen was well-tolerated in people living with uncontrolled gout. The emerging data indicates an overall response rate of 44 percent when adding an additional tolerizing dose of KRYSTEXXA between the first and second biweekly administrations. TRIPLE is the first prospective study evaluating the recommended 'stopping rules' developed to avoid the development of IRs. Results demonstrate that a reduction in the rate of IRs can occur, with IRs from this study associated with less than one percent of the infusions.

- The poster presentation at ACR/ARHP included data from 50 uncontrolled gout patients who received a total of 315 infusions in this multicenter, open-label dosing study.
- Out of 315 doses of KRYSTEXXA administered, only one mild IR occurred (0.3 percent) in a single patient, which did not meet the criteria for anaphylaxis.
- The most common adverse event (AE) reported was a gout flare. A total of 26 patients (52 percent) experienced gout flares.
- The AEs were mostly mild to moderate (92 percent). Eight serious adverse events were reported – three were considered to be unrelated to KRYSTEXXA and five were characterized as a severe gout flare.
- Seven patients (14 percent) discontinued treatment before completing the study.

#### **Treatment with Pegloticase Significantly Decreases Mean Arterial Blood Pressure in Patients with Chronic Gout (abstract [2067](#))**

Data from this post-hoc analysis provides valuable insights on connections between sUA levels and blood pressure for people living with uncontrolled gout treated with KRYSTEXXA. Such patients often have other health conditions that are closely associated with high blood pressure, such as chronic kidney disease.<sup>1</sup>

The analysis of 173 patients with uncontrolled gout included data from two pivotal, six-month clinical trials in which patients were randomized to treatment with KRYSTEXXA every two or four weeks or placebo. Results show that 62.1 percent of patients who received KRYSTEXXA every two weeks, and were characterized as sUA responders by the prespecified primary endpoint, experienced meaningful reductions in mean arterial blood pressure throughout the trials. These reductions were independent of changes in renal function. [A similar analysis was recently presented at the American Society of Nephrology \(ASN\) Kidney Week 2017.](#) While the studies in these analyses were not designed to evaluate change in mean

arterial blood pressure as a clinical endpoint, these findings support further investigation of KRYSTEXXA in blood pressure reduction.

#### **Evidence-Based Development of Criteria for Complete Response in Patients with Chronic Refractory Gout (abstract 2070)**

In a post-hoc analysis of two pivotal, identical, six-month, randomized clinical trials and an open-label study of uncontrolled gout patients, the majority of uncontrolled gout patients treated with KRYSTEXXA who had persistently lower sUA also reached criteria for remission and did so within one year from the initiation of therapy. The trials were controlled up to six months, with a portion of patients continuing in an open-label study and forming the basis of this post-hoc analysis. Forty-two percent of uncontrolled gout patients met the prespecified primary endpoint for complete response, and 85.3 percent of these patients met the published criteria for remission. The mean time from the beginning of the clinical trials to reach remission was 11.5 months. All patients who achieved a remission maintained response until the end of follow-up (mean duration of remission was 507.4 days).

#### **Rapid Tophus Resolution in Chronic Refractory Gout Patients Treated with Pegloticase (abstract 2054)**

Data from a post-hoc analysis of two pivotal, six-month, randomized clinical trials and open-label study indicates rapid resolution of tophi was observed in patients with uncontrolled gout characterized as sUA responders by the prespecified primary endpoint. The trials were controlled up to six months, with a portion of patients continuing in an open-label study and forming the basis of this post-hoc analysis. Serial standardized digital images of 260 tophi were analyzed for 87 patients with uncontrolled gout, 23 of whom were sUA responders, and showed the velocity of tophus reduction was 60.2 mm<sup>2</sup> per month in sUA responders over the course of the trials with a mean time for complete resolution of tophi at 132 days.

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 uncontrolled gout continue to have abnormally high levels of uric acid and continued symptoms despite the use of conventional therapies.

KRYSTEXXA is the only medicine approved by the U.S. Food and Drug Administration (FDA) for the treatment of uncontrolled gout in adult patients.

For more information, please visit [www.KRYSTEXXAHCP.com](http://www.KRYSTEXXAHCP.com)

#### **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.

###### **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](http://www.horizonpharma.com). Follow [@HZNPplc](https://twitter.com/HZNPplc) on Twitter, like us on [Facebook](https://www.facebook.com/horizonpharma) or view careers on our [LinkedIn](https://www.linkedin.com/company/horizonpharma) 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 uncontrolled gout, the potential for dosing strategies to increase effectiveness of KRYSTEXXA, 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, the fact that results in ongoing clinical trials may not support better patient outcomes from the use of KRYSTEXXA, 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.

**References**

<sup>1</sup> National Kidney Foundation. *A to Z Health Guide: Gout, Hyperuricemia and Chronic Kidney Disease*. Web. October 11, 2017. <https://www.kidney.org/atoz/content/gout>

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Source: Horizon Pharma plc