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## Horizon Pharma plc Presents Data on KRYSTEXXA® (pegloticase) for the Management of Refractory Chronic Gout at the 2016 ACR/ARHP Annual Meeting

### Data Demonstrate Patients Defined as "Non-Responders" Achieved Significant Clinical Benefits

DUBLIN, Ireland, Nov. 14, 2016 (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 a retrospective analysis of data from previous pivotal, randomized KRYSTEXXA® (pegloticase) clinical trials demonstrate that refractory chronic gout patients defined as "non-responders" based on serum uric acid levels in the trials still achieved significant clinical benefit despite a loss of response in uric acid levels. These data ([abstract 212](#)) were presented during the American College of Rheumatology (ACR) and the Association of Rheumatology Health Professionals (ARHP) Annual Meeting in Washington D.C. on Sunday, November 13, 2016.

"In a recent survey of U.S. adults living with gout, nearly half said they could not imagine anything more painful than a gout flare, revealing a critical need for education and ongoing study of the available options for managing the condition," said Jeffrey W. Sherman, M.D., FACP, executive vice president, research and development and chief medical officer, Horizon Pharma plc. "Our clinical presence at the ACR meeting this year is the largest for KRYSTEXXA in three years and underscores our drive to expand awareness of this innovative treatment option for refractory chronic gout sufferers."

KRYSTEXXA is the first and only medicine approved by the U.S. Food and Drug Administration 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 where uric acid builds up in the blood and can lead to severe pain and joint destruction, as well as the manifestation of tophi, which are hard, uric acid deposits under the skin that contribute to bone and cartilage destruction. Patients with refractory chronic gout continue to have abnormally high levels of uric acid despite conventional therapies. Refractory chronic gout impacts an estimated 50,000 people in the United States.

"The pivotal clinical trials evaluating KRYSTEXXA provide a wealth of data for health care providers treating people living with refractory chronic gout," said Peter E. Lipsky, M.D., AMPEL BioSolutions, and one of the authors of the poster presentation. "A retrospective look at this data uncovered that patients defined as "non-responders" in the trial actually experienced significant clinical benefits from KRYSTEXXA, with a quarter of non-responders achieving complete tophus resolution at six months."

### Summary of Results

- | Gout symptom improvements were greatest for responders, but also significant for non-responders.
- | 25 percent of non-responders reported complete tophus resolution at six months.
- | Non-responders achieved a statistically significant decrease in gout flares at six months.
- | Non-responders reported improvements from baseline across several meaningful clinical endpoints including Patient Global Assessment, tender and swollen joints and pain.
- | No significant improvements were observed among patients who received placebo.
- | Across the pivotal clinical trials, the most common serious side effects in patients taking KRYSTEXXA were gout flare-ups or attacks, severe allergic reactions, and infusion reactions.

The FDA approval of KRYSTEXXA was based on positive results from two six-month, randomized clinical trials that used uric acid levels to define a "responder." The retrospective analysis presented at the ACR/ARHP annual meeting assessed the clinical efficacy before and after KRYSTEXXA treatment across four groups of clinical trial participants: 36 responders (uric acid levels less than 6.0 mg/dl for 80 percent of the time during extensive monitoring); 24 per-protocol non-responders (received all planned KRYSTEXXA infusions in the clinical trial and had mean uric acid levels greater than 6.0 mg/dl); 49 non-responders (both per-protocol non-responders and those who left the study before uric acid assessments at three and six months); and 43 patients who received placebo.

Responders exhibited mean reductions in uric acid levels to less than 0.5 mg/dL at three and six months. While both groups of non-responders had a transient decrease in uric acid levels that returned to a mean of greater than 6.0 mg/dL by seven weeks, results indicated that these patients had significant clinical benefit.

In addition to the retrospective analysis of the pivotal KRYSTEXXA clinical trials, another study ([abstract 213](#)) was presented evaluating methods for preventing infusion reactions. This was a retrospective review of KRYSTEXXA-treated gout patients since January 2012 who completed at least three infusions. The study compared two different corticosteroids used to prevent infusion reactions: methylprednisolone and hydrocortisone. Results indicate that methylprednisolone pre-infusion therapy may allow for longer KRYSTEXXA therapy duration compared with hydrocortisone. The poster presentation notes that "methylprednisolone use as compared to hydrocortisone for infusion prophylaxis needs further study to determine efficacy and long-term safety."

### **About KRYSTEXXA®**

### **INDICATIONS AND USAGE**

KRYSTEXXA® (pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

Important Limitations of Use: KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

### **IMPORTANT SAFETY INFORMATION**

#### **WARNING: ANAPHYLAXIS and INFUSION REACTIONS; G6PD DEFICIENCY ASSOCIATED HEMOLYSIS and METHEMOGLOBINEMIA**

- | **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 pre-medicated 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.**
- | **Screen patients at risk for G6PD deficiency prior to starting KRYSTEXXA. Hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. Do not administer KRYSTEXXA to patients with G6PD deficiency.**

### **CONTRAINDICATIONS**

- | **Glucose-6-phosphate dehydrogenase (G6PD) Deficiency:** Before starting KRYSTEXXA, confirm patients are not G6PD deficient. Patients at higher risk for G6PD deficiency (e.g., those of African and Mediterranean ancestry) should be screened because of the risk of hemolysis and methemoglobinemia, however any patient could be affected.

### **WARNINGS AND PRECAUTIONS**

- | **Anaphylaxis:** Anaphylaxis occurred in patients treated with 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. 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.
- | **Infusion Reactions:** Infusion reactions occurred in patients treated with KRYSTEXXA. KRYSTEXXA should be administered in a healthcare setting and by healthcare providers prepared to manage infusion reactions. Patients should be premedicated with antihistamines and corticosteroids. Monitor patients closely for signs and symptoms of infusion reactions. In the event of an infusion reaction, the infusion should be slowed, or stopped and restarted at a slower rate. If a severe infusion reaction occurs, discontinue infusion and institute treatment as needed. The risk of an infusion reaction is higher in patients who have lost therapeutic response.
  - | 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.
  - | Concomitant use of KRYSTEXXA and oral urate-lowering agents may blunt the rise of serum uric acid levels. It is recommended that patients discontinue oral urate-lowering agents and not institute therapy with oral urate-

lowering agents while taking KRYSTEXXA.

- 1 **Gout Flares:** An increase in gout flares is frequently observed upon initiation of antihyperuricemic therapy, including treatment with KRYSTEXXA. If a gout flare occurs during treatment, KRYSTEXXA need not be discontinued. Gout flare prophylaxis with a nonsteroidal 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.
- 1 **Congestive Heart Failure:** KRYSTEXXA has not been formally studied in patients with congestive heart failure, but some patients in clinical trials experienced exacerbation. Exercise caution when using KRYSTEXXA in patients who have congestive heart failure, and monitor patients closely following infusion.
- 1 **Re-treatment:** No controlled clinical data is available on the safety and efficacy of re-treatment with KRYSTEXXA after stopping treatment for longer than 4 weeks. Patients receiving re-treatment may be at increased risk for anaphylaxis and infusion reactions and should be monitored carefully.

## ADVERSE REACTIONS

The most commonly reported serious adverse reactions in the pivotal trial with the approved regimen of 8 mg KRYSTEXXA administered every 2 weeks were gout flares, infusion reactions and anaphylaxis. Most common adverse reactions: gout flares (77%), infusion reactions (26%), nausea (12%), contusion or ecchymosis (11%), nasopharyngitis (7%), constipation (6%), chest pain (6%), anaphylaxis (5%) and vomiting (5%). In addition to events occurring in greater than 5%, exacerbation of pre-existing congestive heart failure occurred in 2%.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

Please see [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](http://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 statements regarding the potential of KRYSTEXXA to treat refractory chronic gout patients and Horizon Pharma's intention to expand awareness of KRYSTEXXA. These forward-looking statements are based on management 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 those 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 does not undertake any obligation to update or revise these statements, except as may be required by law.

Contacts:

Investors:

Tina Ventura

Senior Vice President, Investor Relations

[Investor-relations@horizonpharma.com](mailto:Investor-relations@horizonpharma.com)

U.S. Media Contact:

Matt Flesch

Executive Director, Product Communications

[media@horizonpharma.com](mailto:media@horizonpharma.com)

Ireland Media Contact:

Ray Gordon

Gordon MRM

[ray@gordonmrm.ie](mailto:ray@gordonmrm.ie)

 Primary Logo

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