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## **Ultragenyx and Kyowa Kirin Announce Burosumab Receives Positive CHMP Opinion for the Treatment of X-Linked Hypophosphatemia in Children**

### **If approved, Burosumab would be the first targeted disease-modifying treatment for XLH**

TOKYO, LONDON and NOVATO, Calif., Dec. 15, 2017 (GLOBE NEWSWIRE) -- Kyowa Hakko Kirin Co., Ltd. (Kyowa Hakko Kirin), Kyowa Kirin International PLC (Kyowa Kirin International) and Ultragenyx Pharmaceutical Inc. (NASDAQ:RARE), today announced that the Committee for Medicinal Products for Human Use (CHMP), the European Medicines Agency's (EMA) scientific committee, has adopted a Positive Opinion recommending the conditional marketing authorization of burosumab, an anti-FGF23 human monoclonal antibody, for the treatment of X-linked hypophosphatemia (XLH) with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons. XLH is a rare, genetic, chronic and progressive musculoskeletal disorder. If approved, burosumab would be the first therapy that addresses the excess FGF23 activity in XLH.

The CHMP's opinion is now being referred to the European Commission (EC), for a final decision on the grant of a conditional marketing authorization. This decision is expected in the first quarter of 2018 and will apply to all 28 countries of the European Union, Norway, Iceland and Liechtenstein. The conditional authorization requires fulfilment of specific obligations related to the completion of ongoing clinical studies of burosumab in pediatric patients.

"Our scientists at Kyowa Hakko Kirin were the first to discover and succeed in cloning FGF23 and identify the role of the protein in treating phosphate wasting diseases. This prompted a robust research programme and clinical development collaboration with Ultragenyx to develop burosumab, an antibody to FGF23," said Mitsuo Satoh, Ph.D., Executive Officer, Vice President Head of R&D Division of Kyowa Hakko Kirin. "We are pleased to reach this significant regulatory milestone and will continue our scientific journey to help address the medical needs of people with XLH."

Dr. Tom Stratford, President and Chief Executive of Kyowa Kirin International, said: "At Kyowa Kirin International we are fully committed to improving the lives of the many young people across Europe who are living with XLH. We welcome the CHMP's opinion which takes us one step closer to launching burosumab across Europe as the first targeted treatment with the potential to address this often painful and debilitating musculoskeletal condition."

"The positive CHMP opinion is an important step in accelerating patient access to this therapy, which could fundamentally change how this disease is treated," said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx.

Kyowa Hakko Kirin, Kyowa Kirin International, a wholly owned subsidiary of Kyowa Hakko Kirin, and Ultragenyx, have been collaborating in the development and commercialization of burosumab globally, based on the collaboration and license agreement between Kyowa Hakko Kirin and Ultragenyx.

### **Burosumab Regulatory Status**

The EMA's scientific committee adopted a Positive Opinion recommending the conditional marketing authorization of burosumab for the treatment of X-linked hypophosphatemia (XLH) with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons. The CHMP's recommendation is now being referred to the European Commission (EC), which is expected to render its final decision in the first quarter of 2018. The EC typically adheres to the recommendation of the CHMP, but is not obligated to do so.

### **About X-Linked Hypophosphatemia (XLH)**

XLH is a rare, chronic progressive musculoskeletal disorder characterised by renal phosphate wasting caused by excess FGF23 production, and is inherited as an X-linked dominant trait affecting both males and females. XLH is first seen in infants and also affects adults.

In children, XLH causes skeletal disease, leading to lower-extremity deformity and diminished height.

The conventional treatment of XLH consists of multiple daily doses of phosphate and active vitamin D to counteract the excess effects of FGF23 but does not correct the underlying disease.

### **About burosumab**

Burosumab is an investigational recombinant fully human monoclonal IgG1 antibody, discovered by Kyowa Hakko Kirin, against the phosphaturic hormone fibroblast growth factor 23 (FGF23). FGF23 is a hormone that reduces serum levels of phosphorus and active vitamin D by regulating phosphate excretion and active vitamin D production by the kidney. Burosumab is being developed to treat XLH and tumor-induced osteomalacia (TIO), diseases characterized by excess levels of FGF23. Phosphate wasting in XLH and TIO is caused by excessive levels and activity of FGF23. Burosumab is designed to bind to and thereby inhibit the biological activity of FGF23. By blocking excess FGF23 in patients with XLH and TIO, burosumab is intended to increase phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

In the United States, the U.S. Food and Drug Administration (FDA) is currently reviewing the Biologics License Application for burosumab to treat pediatric and adult patients with XLH, and has set a Prescription Drug User Fee Act (PDUFA) action date of April 17, 2018.

A clinical program studying burosumab in adults and pediatric patients with XLH is ongoing. Burosumab is also being developed for TIO, a disease characterized by typically benign tumors that produce excess levels of FGF23, which can lead to severe osteomalacia, fractures, bone and muscle pain, and muscle weakness.

### **About Kyowa Kirin**

Kyowa Hakko Kirin Co., Ltd. is a research-based life sciences company, with special strengths in biotechnologies. In the core therapeutic areas of oncology, nephrology and immunology/allergy, Kyowa Hakko Kirin leverages leading-edge biotechnologies centered on antibody technologies, to continually discover innovative new drugs and to develop and market those drugs world-wide. In this way, the company is working to realize its vision of becoming a Japan-based global specialty pharmaceutical company that contributes to the health and wellbeing of people around the world.

Kyowa Kirin International PLC is a wholly owned subsidiary of Kyowa Hakko Kirin and is a rapidly growing specialty pharmaceutical company engaged in the development and commercialization of prescription medicines for the treatment of unmet therapeutic needs in Europe and the United States. Kyowa Kirin International is headquartered in Scotland.

You can learn more about the business at: [www.kyowa-kirin.com](http://www.kyowa-kirin.com).

### **About Ultragenyx**

Ultragenyx is a clinical-stage biopharmaceutical company committed to bringing to market novel products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. Founded in 2010, the company has rapidly built a diverse portfolio of product candidates with the potential to address diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies.

The company is led by a management team experienced in the development and commercialization of rare disease therapeutics. Ultragenyx's strategy is predicated upon time and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency.

For more information on Ultragenyx, please visit the company's website at [www.ultragenyx.com](http://www.ultragenyx.com).

### **Forward-Looking Statements**

*Except for the historical information contained herein, the matters set forth in this press release, including statements relating to Ultragenyx's expectations regarding future regulatory interactions, the potential timing and success of filings for regulatory approvals, potential indications for its product candidates and plans for its clinical programs and clinical studies, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in the clinical drug development process, such as the regulatory approval process, the timing of regulatory filings, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations and the availability or commercial potential of our drug candidates. Ultragenyx undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of Ultragenyx in general,*

*see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 3, 2017, and its subsequent periodic reports filed with the Securities and Exchange Commission.*

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