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Ultragenyx Reports Positive Interim Data from Phase 2 Study of KRN23 for the Treatment of Tumor-Induced Osteomalacia

Company to host conference call at 11am ET Monday, September 19 to discuss results

NOVATO, Calif., Sept. 18, 2016 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ:RARE), a biopharmaceutical company focused on the development of novel products for rare and ultra-rare diseases, today announced positive interim data from the Phase 2 study of KRN23 for the treatment of tumor-induced osteomalacia (TIO). Interim data at 24 weeks from the first eight patients, including one patient with epidermal nevus syndrome (ENS), demonstrated that KRN23 improved serum phosphorus levels and bone metabolism measures. Ultragenyx is conducting the Phase 2 study under a collaboration and license agreement with Kyowa Hakko Kirin to develop and commercialize KRN23. These data were presented today at the American Society for Bone and Mineral Research (ASBMR) 2016 Annual Meeting.

"Patients with TIO have substantial hypophosphatemia, osteomalacia and fractures," said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. "These data support that KRN23 could potentially reverse some of these symptoms and improve bone health in patients."

Mean serum phosphorus, renal phosphate reabsorption (TmP/GFR) and serum 1,25 dihydroxy vitamin D levels increased over 24 weeks of treatment. Before KRN23 treatment and after washout with any oral phosphate treatment, the mean serum phosphorus level was 1.7 mg/dL, well below the lower limit of normal of 2.5 mg/dL. The mean serum phosphorus level entered the normal range within one week of treatment, and was maintained in the low normal range from week 10 to week 24 of treatment. Overall, the improvement in serum phosphorus and other bone mineral metabolism measures observed in this study to date is generally consistent with what has been observed in studies of KRN23 in pediatric and adult patients with X-linked hypophosphatemia (XLH).

Of the seven patients who responded, six patients showed an improvement in bone mineral density at 24 weeks of treatment. Bone turnover markers, including Procollagen type 1 N-terminal propeptide (P1NP) and C-telopeptide of type I collagen (CTX-1), showed a statistically significant increase. One patient completed 48 weeks of treatment, at which time bone biopsies indicated an improvement from severe osteomalacia at baseline to mild osteomalacia at 48 weeks. The same patient showed resolution of four fractures at 24 weeks of treatment, determined by bone scan as previously disclosed. Bone mineral density for this patient improved 2% and 3% in the lumber spine and total hip, respectively. Bone biopsy and bone scan data for additional patients will be available at a later date.

Adverse events occurred in all patients. Treatment-related adverse events were observed in three patients (38%), and included Vitamin D deficiency and rash as previously disclosed, and dysgeusia, all mild in grade. There was one serious adverse event of neoplasm progression, which occurred in one patient with pre-existing metastatic spindle sarcoma who did not respond and has discontinued treatment. No injection site reactions were observed. Two patients had restless leg syndrome, one of whom had symptoms suggestive of worsening pre-existing restless leg syndrome. No clinically meaningful changes were observed in mean serum calcium, urinary calcium and in serum intact parathyroid hormone.

Conference Call Details

Ultragenyx will host a conference call on Monday, September 19 at 11am ET during which Dr. Kakkis will discuss results of the KRN23 studies being presented at the ASBMR Annual Meeting. The live and replayed webcast of the call will be available through the company's website at http://ir.ultragenyx.com/events.cfm. To participate in the live call by phone, dial 855-797-6910 (USA) or 262-912-6260 (international) and enter the passcode 83882106. The replay of the call will be available for one year.

Phase 2 Study Design

The open-label, dose-finding Phase 2 clinical study is evaluating the safety and efficacy of KRN23 in 17 adult patients. The primary objectives of the study are to establish the dose, and assess the safety profile and efficacy of treatment with KRN23 in adults with TIO and ENS whose tumors or lesions cannot be resected. Patients receive subcutaneous injections of KRN23

once every four weeks for 48 weeks. All patients begin treatment with KRN23 at a starting dose of 0.3 mg/kg. Doses are then titrated in an effort to achieve a target fasting serum phosphorus range of 2.5 to 4.0 mg/dL. After completing the initial 48-week treatment period of the study, patients may continue into a planned treatment extension period in which they receive KRN23 treatment for up to an additional 96 weeks. The co-primary endpoints include: the proportion of patients achieving mean peak serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL), as averaged between baseline and week 24; and the percent change from baseline in excess osteoid after 48 weeks of treatment. Preliminary clinical effects of KRN23 treatment will be evaluated by radiographic assessments, muscle strength, walking ability, and by patient-reported measures of pain, disability, and quality of life. Markers of bone health and changes in serum phosphorus and other biochemical measures are also followed.

KHK is conducting a separate Phase 2 study evaluating the safety and efficacy of KRN23 in 12 adult patients in Japan.

About TIO

TIO, and a skin lesion variant, epidermal nevus syndrome (ENS)-associated osteomalacia, are caused by typically benign tumors or lesions that produce excess levels of FGF23, causing phosphate wasting in the urine that leads to severe hypophosphatemia, osteomalacia, muscle weakness, fatigue, bone pain, and fractures. The symptoms rapidly resolve if the causal tumors or lesion can be resected; however, there are cases in which resection is not feasible or recurrence of the tumor occurs after resection. In patients for whom the tumor or lesion is inoperable, the current treatment consists of oral phosphate and/or vitamin D replacement. Efficacy of this treatment is often limited, as it does not treat the underlying disease and its benefits must be balanced with monitoring for potential risks such as nephrocalcinosis, hypercalciuria, and hyperparathyroidism. There are an estimated 500-1,000 patients with TIO in the United States, and approximately half of all cases are inoperable.

About KRN23

KRN23 is an investigational recombinant fully human monoclonal IgG1 antibody, discovered by Kyowa Hakko Kirin, against the phosphaturic hormone fibroblast growth factor 23 (FGF23). It is being developed by Ultragenyx and Kyowa Hakko Kirin to treat XLH and TIO, diseases characterized by excess activity of FGF23. FGF23 is a hormone that reduces serum levels of phosphorus and vitamin D by regulating phosphate excretion and vitamin D production by the kidney. Phosphate wasting in XLH and TIO is caused by excessive levels and activity of FGF23. KRN23 is designed to bind to and thereby inhibit the excessive biological activity of FGF23. By blocking excess FGF23 in patients with XLH and TIO, KRN23 is intended to increase phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

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.

About Kyowa Hakko Kirin

Kyowa Hakko Kirin is a leading biopharmaceutical company in Japan focusing on its core business area of oncology, nephrology, and immunology/allergy. Kyowa Hakko Kirin leverages antibody-related leading-edge technologies to discover and develop innovative new drugs aiming to become a global specialty pharmaceutical company which contributes to the health and well-being of people around the world.

For more information, please visit www.kyowa-kirin.com.

Forward-Looking Statements

Except for the historical information contained herein, the matters set forth in this press release, including statements regarding Ultragenyx's expectations regarding the timing of release of additional data for its product candidates, plans to initiate additional studies for its product candidates and timing regarding these studies, plans regarding ongoing studies for

existing programs and its intent to file for conditional approval, 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, including the regulatory approval process, the timing of our regulatory filings, and other matters that could affect the success of our drug development programs, including KRN23. 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 the Company in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 9, 2016, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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