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

NOVATO, Calif., April 21, 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). Initial data from the first eight patients in the study, including one patient with epidermal nevus syndrome (ENS), demonstrated that KRN23 improved serum phosphorus levels and other bone metabolism measures. The study has been expanded to enroll approximately 15 patients, and enrollment is ongoing.

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. After KRN23 treatment began, six of the eight patients achieved serum phosphorus levels that entered the normal range. The dose continues to be titrated up in one of the two patients whose serum phosphorus levels have increased but not entered the normal range. Renal phosphate reabsorption (TmP/GFR) and serum 1,25 dihydroxy vitamin D levels also increased in seven of the eight patients. One patient did not demonstrate an improvement in these markers. 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 eight patients enrolled, the two patients who completed 24 weeks of treatment showed an improvement in bone mineral density, and one of these two patients showed early evidence of fracture resolution, determined via bone scan. Additional bone data will be available in the second half of 2016.

"The data show that KRN23 can restore serum phosphorus levels to normal ranges and may have a meaningful effect on bone health in patients," said Sunil Agarwal, M.D., Chief Medical Officer of Ultragenyx. "We now have data in two diseases, TIO and XLH, suggesting that KRN23 binds to and inhibits the activity of excess fibroblast growth factor 23 (FGF23), the hormone that leads to phosphate-wasting in these patients."

There have been no serious adverse events. Treatment-emergent adverse events were observed in seven patients (87.5%). Treatment-emergent adverse events occurring in two or more patients were primarily musculoskeletal disorders including pain in extremity, arthralgia, and musculoskeletal pain consistent with the symptoms typically seen in patients with TIO and ENS. Two of the eight patients (25%) had treatment-related adverse events that were possibly/probably related, including Vitamin D deficiency and rash, both of which were mild in grade. No injection site reactions were observed. Two subjects reported 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. One patient had serum phosphorus levels above the upper limit of normal at three weeks of treatment that returned to the normal range by week four after dose reduction, and has remained in the normal range.

Phase 2 Study Design

The open-label, dose-finding Phase 2 clinical study will evaluate the safety and efficacy of KRN23 in approximately fifteen 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. 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 (48 weeks), patients may continue into a planned treatment extension period in which subjects 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.

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 and FGF23

KRN23 is an investigational recombinant fully human monoclonal IgG1 antibody against the phosphaturic hormone FGF23 being developed to treat TIO and XLH, both of which are 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. KRN23 is designed to bind to and thereby inhibit the excessive biological activity of FGF23. By blocking excess FGF23, KRN23 is intended to restore normal phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium. KRN23 was discovered by Kyowa Hakko Kirin Co., Ltd., and Ultragenyx and Kyowa Hakko Kirin entered into a collaboration and license agreement in August 2013 to develop and commercialize KRN23.

About Ultragenyx

Ultragenyx is a clinical-stage biotechnology 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 timing of release of additional data, 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 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 the Company in general, see Ultragenyx's Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 26, 2016, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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