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Ultragenyx Announces Initiation of a Phase 2 Study of KRN23 for Pediatric X-Linked Hypophosphatemia in the US and EU

NOVATO, Calif., July 1, 2014 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (Nasdaq:RARE), a biopharmaceutical company focused on the development of novel products for rare and ultra-rare diseases, announced the first patient screened and enrolled in the Phase 2 study of the human monoclonal anti-FGF23 antibody KRN23 (UX023) in pediatric patients with X-linked hypophosphatemia (XLH). XLH is an inherited metabolic bone disease characterized by short stature, skeletal deformities, bone pain, fractures, and muscle weakness.

"The initiation of the Phase 2 study of KRN23 in pediatric XLH patients is a significant step forward in our overall development plan for this debilitating bone disease," commented Emil D. Kakkis, M.D., Ph.D., Ultragenyx's Chief Executive Officer. "Completed studies in adults with XLH show KRN23's effect in increasing phosphate levels and bone remodeling. Due to the high rate of growth and bone formation during childhood and the critical role phosphate plays in bone mineralization, pediatric patients with XLH may have the greatest potential for improvement from treatment with KRN23."

The multi-center, randomized, open-label, dose-finding Phase 2 clinical study will evaluate safety and efficacy in approximately 30 prepubertal pediatric XLH patients. The primary objectives of the study are to identify a dose and dosing regimen and to establish the safety profile of treatment with KRN23 in pediatric XLH patients. Preliminary clinical effects of KRN23 treatment on bone health and deformity as measured by radiographic assessments, growth, muscle strength, and motor function will also be assessed, as well as markers of bone health and patient-reported outcomes of pain, disability, and quality of life. The study has been evaluated and accepted for conduct by the United States Food and Drug Administration (FDA), the United Kingdom Medicinal and Health Regulatory Authority (MHRA), and the Dutch Medicines Evaluation Board (CBG-MEB).

The study will consist of a 16-week individual dose-titration period followed by a 48-week treatment period. The goal of the dose-titration period is to identify the individualized dose of KRN23 required to achieve stable serum phosphorus levels in the target range. Patients will be divided into three cohorts of escalating starting dose levels of KRN23 with either monthly or biweekly dosing regimens. At the end of the 16-week dose-titration period, patients will receive their individually-optimized dose of KRN23 on a monthly or biweekly basis for the 48-week treatment period. An interim analysis of safety and pharmacodynamic data will be conducted after 24 weeks of the treatment period.

In a recent meeting with Ultragenyx, the FDA agreed that blinded radiographic assessments of changes in bone abnormalities, i.e. rickets and bowing, and changes in growth may be used as primary endpoint measures in the pediatric development program and a potential Phase 3 study. The FDA also indicated that a Phase 3 study in pediatric patients could be open-label, but recommended inclusion of a standard of care control arm for comparison on a non-inferiority basis. The final design of a pediatric Phase 3 study would be determined once sufficient safety and efficacy data are available and after further consultation with the FDA. Ultragenyx also intends to continue clinical development in the adult population in parallel with the pediatric program.

About X-linked Hypophosphatemia (XLH)

XLH is a disorder of phosphate metabolism caused by phosphate wasting in the urine leading to severe hypophosphatemia. XLH is the most common heritable form of rickets that is inherited as an X-linked dominant trait affecting both males and females, though some reports indicate that the disease may be more severe in males. Studies suggest there are approximately 12,000 XLH patients in the United States. XLH is a distinctive bone disease characterized by inadequate mineralization of bone that leads to a spectrum of abnormalities, including rickets, progressive bowing of the leg, osteomalacia, bone pain, waddling gait, short stature, gross motor impairment, muscle weakness, osteopenia, frequent/poorly healing microfractures, spinal stenosis, enthesopathy, and osteoarthritis.

Most patients are managed using oral phosphate replacement and vitamin D (calcitriol) therapy, which requires frequent divided doses and careful medical monitoring. It is partially effective at reducing rickets, but it does not improve growth and can be challenging to optimize the dose without increasing the risk of depositing phosphate-calcium precipitates in the kidneys (nephrocalcinosis).

About KRN23 and FGF23

KRN23 is an investigational recombinant fully human monoclonal IgG1 antibody against the phosphaturic hormone fibroblast growth factor 23 (FGF23) being developed to treat XLH, a disease 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 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, 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. Ultragenyx and Kyowa Hakko Kirin Co., Ltd. (KHK) entered into a collaboration and license agreement in August 2013 to develop and commercialize KRN23.

About Ultragenyx

Ultragenyx is a development-stage biotechnology company committed to bringing to market novel products for the treatment of rare and ultra-rare diseases, with an initial 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 http://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 the potential for improvement of pediatric patients with XLH as a result of treatment with KRN23, the design of the study, the number of patients who will participate in the study, the timing of completing an interim analysis of the data,expectations regarding initiation and design of a pivotal Phase 3 program, and clinical development of KRN23 in adult patients with XLH, 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 (including the possibility that the FDA could change its prior recommendation regarding the design of a Phase 3 study for KRN23 or make additional comments in further discussions with the Company), the timing of our regulatory filings and other matters that could affect the availability or commercial potential of our drug candidate. 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 for the quarter ended March 31, 2014 filed with the Securities and Exchange Commission on May 12, 2014, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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