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Ultragenyx Announces Results From Phase 1/2 Study of KRN23 in X-linked Hypophosphatemia in Adults

Treatment With KRN23 Induces a Sustained Increase in Serum Phosphorus and Increases in Bone Remodeling Markers

NOVATO, Calif., June 24, 2014 (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 the presentation of results from a multiple-dose study, conducted by Kyowa Hakko Kirin Pharma, Inc. (KKP), of the investigational anti-FGF23 monoclonal antibody KRN23 (UX023) in adult 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 data was presented at the 2014 ICE/ENDO joint meeting of The Endocrine Society and The International Congress of Endocrinology in Chicago.

"We are pleased with the results of the Phase 1/2 study of KRN23 in adult patients with XLH," commented Emil D. Kakkis, M.D., Ph.D., Ultragenyx's Chief Executive Officer. "Based on observed improvements in phosphate metabolism, bone remodeling markers, and certain quality of life measures, we are encouraged by the potential for KRN23 to treat the underlying cause of bone disease in both adult and pediatric patients with XLH."

A multiple-dose Phase 1/2 study (INT-001) with up to four escalating doses from 0.05 mg/kg to 0.6 mg/kg was completed in 28 adult XLH patients. The study assessed the safety and tolerability of subcutaneous injections of KRN23 given once every four weeks.

The efficacy data from the Phase 1/2 study demonstrate that blocking excess FGF23 increases urinary phosphorus reabsorption, serum phosphorus levels, and 1,25 dihydroxy vitamin D levels. Repeat doses with KRN23 over four months led to an increase in serum phosphorus in 100% of patients, with approximately 89% of patients reaching the low end of the normal range. Peak mean serum phosphorus increased to 3.03 ± 0.42 mg/dL after the fourth dose, which is an approximately 60% increase from the mean of 1.89 ± 0.33 mg/dL at baseline. Comparable increases were observed in mean reabsorption of phosphate from the urine (TmP/GFR) and mean serum 1,25 dihydroxy vitamin D levels.

Increases in bone remodeling markers were also observed, including markers of bone formation and bone resorption. The increase in P1NP (procollagen type I N propeptide) from baseline was statistically significant ($p < 0.05$) after all doses and the increase in osteocalcin was statistically significant ($p < 0.05$) after the fourth dose. Increases in BALP (bone alkaline phosphatase) and CTx (carboxy terminal cross-linked telopeptide of type I collagen) were also observed. These data support the concept that KRN23's impact on improving phosphate metabolism will improve bone remodeling, a critical part of creating strong, properly-formed bones.

Patients completed two quality of life questionnaires at baseline and after the fourth dose; mean scores improved for all SF-36v2[1] and WOMAC[2] scales, consistent with an improvement in health status for both instruments, although these were not blinded assessments. For SF-36v2, statistically significant increases from baseline were observed in the role limitations due to physical health, bodily pain, and physical component summary scales. For WOMAC, statistically significant increases from baseline were observed in the physical functioning and stiffness scales. Stiffness is one of the major symptoms of XLH in adult patients. These findings will be evaluated objectively in a future randomized controlled study.

There were no significant changes in parathyroid hormone, serum calcium, or urinary calcium excretion, consistent with the Phase 1 data showing that KRN23 can specifically improve phosphate control without interfering with calcium control. The most common adverse events were nasopharyngitis, joint pain, diarrhea, back pain, and restless leg syndrome. Joint pain and back pain are both known symptoms of XLH in adults. There were no serious adverse events related to treatment or renal or cardiac tissue calcification. One patient discontinued treatment due to injection site reaction. No anti-KRN23 antibodies were observed.

In addition to the four-dose Phase 1/2 study (INT-001) presented at ICE/ENDO, a long-term Phase 1/2 study (INT-002) was completed to evaluate KRN23 treatment for an additional 12 doses in 22 of the patients from INT-001. Administration of KRN23 continued to show a favorable safety profile and sustained improvements in phosphate metabolism and other measures. Data from the long-term Phase 1/2 study is expected to be presented at the American Society for Bone and Mineral Research

(ASBMR) Annual Meeting in September.

Based on the Phase 1 and Phase 1/2 study results to date, Ultragenyx and Kyowa Hakko Kirin Co., Ltd. (KHK) plan to initiate a Phase 2 study of KRN23 in pediatric patients in 2014 and expect to continue the clinical development of KRN23 in adults with XLH.

[1]Medical Outcomes Study 36-item Short Form, Version 2 (SF-36v2) is comprised of eight scales measuring physical function, role limitations due to physical health, bodily pain, general health perceptions, vitality, role limitations due to emotional problems, and mental health, as well as physical component summary and mental component summary composite scores.

[2]Western Ontario and McMaster University Osteoarthritics Index (WOMAC) is comprised of three scales measuring pain, stiffness, and physical functioning.

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 IgG_1 antibody discovered by KHK 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 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 KRN23 to treat the underlying cause of bone disease in adult and pediatric patients with XLH, the effects of blocking excess FGF23, the effects of improving phosphate metabolism, the evaluation of findings in future studies, the timing of release of additional data, plans to conduct additional studies (and anticipated timing of the initiation of such studies), the number of patients in the United States who have XLH and the intended result of administration of KRN23, 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, that these results (which were in adult patients) may not translate into similar safety or efficacy in pediatric patients, 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 Quarterly Report on Form 10-Q 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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