Ultragenyx and Kyowa Kirin International Announce Positive Data from Paediatric Phase 2 Studies of Burosumab (KRN23) in X-Linked Hypophosphatemia

Sustained reduction in bone disease and improvement in growth through 64 weeks of treatment and sustained effect on bone mineral metabolites in patients under 5 years old

Novato, CA and London, UK— April 6, 2017 — Ultragenyx Pharmaceutical Inc. (NASDAQ:RARE) and Kyowa Kirin International PLC (KKI), a wholly owned subsidiary of Kyowa Hakko Kirin Co., Ltd. (Kyowa Hakko Kirin), today announced positive 64-week data from a paediatric Phase 2 study of burosumab (KRN23) for the treatment of X-linked hypophosphatemia (XLH) in children aged five to 12 years of age. The data demonstrated that serum phosphorus levels, rickets, growth rates, and other functional outcomes improved with burosumab, and these treatment effects were sustained through 64 weeks of treatment. In addition, interim 24-week data from the separate paediatric Phase 2 study in patients aged one to five years demonstrated that burosumab increased serum phosphorus levels into the low normal range. Adverse events were consistent with what has been previously observed for burosumab for the treatment of XLH. Ultragenyx is conducting the studies under a collaboration and licence agreement with Kyowa Hakko Kirin to develop and commercialise burosumab.

"These data support the potential for burosumab to treat XLH in paediatric patients, and show that treatment with burosumab can improve bone health and growth in children who have this debilitating disease," said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. "The first results in the younger under-5 year old group are consistent with what we have seen in older children, supporting the potential value of early treatment initiation."

"The data from these paediatric studies are encouraging and support our aim to contribute to the health and wellbeing of people through innovative drug discovery and commercialisation of medicinal products," said Dr. Tom Stratford, President and CEO of KKI. "We are confident that burosumab has the potential to address a clear unmet medical need in the treatment of XLH."

Phase 2 XLH Study in five to 12 Year Olds

The randomised, multicentre, open-label, dose-finding study enrolled 52 patients between five and 12 years old, 49 of whom had been on currently available therapy (oral phosphate/active vitamin D therapy) for an average of approximately seven years prior to entering the study. All patients have completed the full 64-week dose-titration and treatment period. A subset of these patients (n=34) were pre-specified as having higher RSS scores, defined by baseline total RSS scores of $\geq$ 1.5.

Metabolic Measures

Patients demonstrated increases in mean serum phosphorus, renal phosphate reabsorption (TmP/GFR) and serum 1,25 dihydroxy vitamin D levels through 64 weeks of treatment. Patients in both dosing groups had mean serum phosphorus levels in the low normal range through 64 weeks of treatment, demonstrating that phosphate wasting, the underlying cause of the disease, improved and patients were able to maintain increased serum phosphorus levels.

Bone Disease Results

Thacher Rickets Severity Scoring (RSS)

Rickets severity was assessed using the RSS scoring system. There was a statistically significant improvement in rickets scores in all groups at 64 weeks, with the greatest improvements in patients with higher baseline rickets scores (RSS ≥1.5) who received bi-weekly dosing of burosumab. Overall, patients (n=52) had a 51% reduction in RSS score ($p < 0.0001$). Patients with higher baseline rickets scores (n=34) had a 59% reduction in RSS score ($p < 0.0001$). Patients who were dosed bi-weekly (n=26) had a 58% reduction in RSS score ($p < 0.0001$). Patients with higher baseline rickets scores who were dosed bi-weekly (n=17) had a 62% reduction in RSS score ($p < 0.0001$).

Radiographic Global Impression of Change (RGI-C) Scale

The change in the severity of rickets was assessed by the RGI-C score. Data show significant improvement in rickets in all groups at 64 weeks. Overall, all patients (n=52) experienced a mean improvement in RGI-C score of +1.57 ($p< 0.0001$) and those patients with higher baseline rickets scores (n=34) experienced a mean improvement of +1.98 ($p< 0.0001$). Within the higher severity subset, 77% (26/34) experienced substantial healing (score $\geq$2). Patients who were dosed bi-weekly (n=26) experienced a mean improvement in RGI-C score of +1.62 ($p< 0.0001$). Patients with higher baseline rickets scores who were dose bi-weekly (n=17) showed a mean improvement of +2.08 ($p< 0.0001$) (substantial healing) and 82% experienced substantial healing.

Growth Velocity

Patients with higher baseline rickets scores showed more growth impairment (baseline height percentile= 5.84), and these patients demonstrated greater improvement in growth. Among all patients (n=52), growth velocity improved by a mean of +0.55 cm/year ($p=0.0376$), and there was 0.15 change in height z-score ($p<0.0001$). Patients with higher baseline rickets scores had a +0.86 cm/year improvement in growth velocity ($p=0.0175$) and a 0.17 change in height z-score ($p=0.0016$). Patients who were dosed bi-weekly (n=26) experienced a +0.73 cm/year change in growth velocity ($p=0.0160$) and a 0.18 change in height z-score ($p=0.0002$). Patients with higher baseline rickets scores who were dosed bi-weekly (n=17) had a +1.11 cm/year change in growth velocity ($p=0.0076$) and a 0.18 change in height z-score ($p=0.0063$).

Functional Measurements: 6 Minute Walk Test (6MWT) and Patient Reported Outcomes (PROs)

Patients with walking impairment at baseline (defined by < 80% predicted normal walk distance in 6MWT) in the bi-weekly dosing group (n=14) achieved a mean increase of 85 meters ($p<0.0001$).

Functional disability scores were measured with the Pediatric Orthopedic Society North America/Pediatric Outcome Data Collection Instrument (POSNA/PODCI). When evaluating the Global score of all five domains in those patients with substantial impairment at baseline (n= 28), defined as baseline scores < 40 or one standard deviation below the normalized score of 50), a mean improvement of +14.1 ($p< 0.0001$) was observed. Though the magnitude of these changes in

functional measurements are substantial, any conclusions must be tempered by the fact that these data are from an uncontrolled, open-label study.

Safety and Tolerability

Approximately 65% of patients had injection site reactions, all of which were considered mild. There was one previously reported serious adverse event considered possibly treatment-related. This was a patient with fever and muscle pain who improved without complication and is still in the study. There have been no deaths or discontinuations from the study. No clinically meaningful changes were observed in mean serum calcium, urinary calcium and in serum intact parathyroid hormone. None of the patients had serum phosphorus levels above the upper limit of normal at any time point. No clinically significant changes were observed in renal ultrasounds pre- and post-treatment.

Phase 2 XLH Study in One to Five Year Olds

The multicentre, open-label Phase 2 study enrolled 13 children between the ages of one and five years old (mean age 2.9 years), all of whom have previously been on oral phosphate/active vitamin D therapy. The 64-week study is assessing the safety, pharmacodynamics, and efficacy of burosumab administered every 2 weeks at a starting dose of 0.8mg/kg, which can be increased to 1.2mg/kg at any time during the study. All patients have completed 24 weeks of treatment. Patients demonstrated increases in mean serum phosphorus, and maintained levels in the low normal range through 24 weeks of treatment. Patients also demonstrated increases in serum 1,25 dihydroxy vitamin D levels, and significant decreases in alkaline phosphatase levels. Adverse events were consistent with what has been previously observed for burosumab for the treatment of XLH. Approximately 23% of patients had injection-site reactions, all of which were considered mild. There have been no deaths or discontinuations from the study.

About Burosumab (KRN23)

Burosumab is an investigational recombinant fully human monoclonal IgG_1 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 tumour-induced osteomalacia (TIO), diseases characterised by excess activity of FGF23. FGF23 is a hormone that reduces serum levels of phosphorus by increasing renal phosphate excretion. FGF23FGF23 also reduces active vitamin D production by the kidney. Burosumab is designed to bind to and thereby inhibit the excessive biological activity of FGF23. By blocking excess FGF23 in patients with XLH and TIO, burosumab increases phosphate reabsorption from the kidney and increases the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

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

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 Kirin

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

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 centred 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 realise its vision of becoming a Japan-based global specialty pharmaceutical company that contributes to the health and wellbeing of people around the world.

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 ongoing or additional studies for its product candidates and timing regarding these 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 our 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 the company in general, see Ultragenyx's Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 17, 2017, and its subsequent periodic reports filed with the Securities and Exchange Commission.