Kyowa Hakko Kirin Announces First Patient Enrolled Global Phase 3 Study of KRN23 in Pediatric Patients with X-Linked Hypophosphatemia (XLH)

Tokyo, October 26th, 2016 -- Kyowa Hakko Kirin Co., Ltd. (Tokyo; 4151 President and CEO: Nobuo Hanai; "Kyowa Hakko Kirin") today announced the initiation of the Phase 3 study of KRN23 for the treatment of pediatric patients with X-linked hypophosphatemia (XLH). Kyowa Hakko Kirin and Ultragenyx entered into a collaboration and license agreement in August 2013 to develop and commercialize KRN23.

The Phase 3 study is a randomized, open-label clinical study comparing the efficacy and safety of KRN23 to oral phosphate and active vitamin D therapy. The study will enroll approximately 60 patients ages one through 12 in the US, EU, Canada, Japan, and Korea. The primary endpoint is the change in rickets at 40 weeks, assessed by the radiographic global impression of change (RGI-C) scale. Secondary endpoints include additional rickets assessments using the RGI-C scale and the Thacher Rickets Severity Scoring (RSS) system, changes in growth velocity and height, pharmacodynamic assessments, walking ability, patient reported outcomes assessing pain, fatigue and physical function, and safety. All patients were previously treated with oral phosphate and active vitamin D therapy, and go through a 7-day washout period prior to randomization. Patients in the KRN23 treatment group receive a starting dose of 0.8 mg/kg administered biweekly, and the dose may be increased up to 1.2 mg/kg.

An ongoing clinical program in XLH includes phase 3 studies in adults and phase 2 and 3 studies in pediatric patients. KRN23 is also being developed for tumor-induced osteomalacia (TIO), a disease characterized by typically benign tumors that produce excess levels of FGF23, which can lead to severe osteomalacia, fractures, bone and muscle pain, and muscle weakness.

The Kyowa Hakko Kirin Group companies strive to contribute to the health and well-being of people around the world by creating new value through the pursuit of advances in life sciences and technologies.

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 (the softening and weakening of bones), that is inherited as an X-linked dominant trait affecting both males and females. XLH is a distinctive 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, frequent/poorly healing pseudofractures, spinal stenosis, enthesopathy, and osteoarthritis. Nearly all pediatric patients and most adult patients are managed using oral phosphate replacement and active vitamin D (calcitriol) therapy, which requires multiple divided doses each day and monitoring for potential risks such as nephrocalcinosis, hypercalciuria, and hyperparathyroidism.

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 active vitamin D by regulating phosphate excretion and active 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.