Ultragenyx and Kyowa Kirin Announce FDA Approval of Crysvita® (burosumab-twza) for the Treatment of Children and Adults with X–Linked Hypophosphatemia (XLH)

First Approved Therapy for XLH in the U.S.; Only Treatment that Targets the Underlying Cause of this Rare, Hereditary, Lifelong Disease

Novato, Calif., Tokyo, Japan, and London, UK, April 17/18, 2018: Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development of novel products for rare and ultra-rare diseases, Kyowa Hakko Kirin Co. Ltd (Kyowa Hakko Kirin), and Kyowa Kirin International PLC (Kyowa Kirin International) today announced that the U.S. Food and Drug Administration (FDA) has approved Crysvita® (burosumab-twza) for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients one year of age and older. Crysvita is an antibody that blocks fibroblast growth factor 23 (FGF23), a hormone that causes phosphate urinary excretion and suppresses active vitamin D production by the kidney.

“Patients now have an approved breakthrough therapy that can help correct the underlying disease, transforming the treatment of XLH and reducing related bone disease in both children and adults living with this disease,” said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. “This milestone represents Ultragenyx’s second approved therapy in less than six months and validates our strategy to rapidly transform good science into effective therapies for rare diseases. This approval would not have been possible without the patients, their families and clinicians who participated and I would like to thank them for their commitment and dedication.”

XLH is a rare, hereditary, progressive and lifelong skeletal disorder characterized by renal phosphate wasting caused by excess FGF23 production. It affects both children and adults. In children, XLH causes rickets that leads to lower-extremity deformity, delayed growth and decreased height. Adults with XLH have an increased risk of fractures. Crysvita is designed to bind the excess FGF23 in these patients, normalizing phosphorus levels, improving bone mineralization, improving rickets in children and healing fractures in adults.

“The approval of Crysvita is truly a watershed moment for patients with X-linked hypophosphatemia as it is the first therapy directed toward correction of renal phosphate wasting,” said Tom Carpenter, M.D., the lead study investigator, Director of the Yale Center for X-Linked Hypophosphatemia, and Professor of Pediatric Endocrinology at Yale University School of Medicine. “By targeting this mechanism Crysvita leads to sustained improvements in phosphate metabolism with concurrent repair of the skeleton, even after prior treatment with conventional approaches. Most importantly, the dosing regimen for Crysvita is far less burdensome than for currently available therapies and should be readily acceptable by families. I expect it to revolutionize the care of patients with XLH.”

Dr Tom Stratford, President and Chief Executive Officer of Kyowa Kirin International, said: "This is excellent news for people affected by XLH and their families. Coming close behind the granting of a European Marketing Authorisation for Crysvita in children, this means that even more patients who suffer from this often debilitating condition can benefit from this medicine."

The FDA previously granted Crysvita a Breakthrough Therapy Designation for the treatment of XLH in pediatric patients one year of age and older, and evaluated Crysvita with Priority Review, which is reserved for drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness.

With this approval, the FDA issued a Rare Pediatric Disease Priority Review Voucher, which confers priority review to a subsequent drug application that would not otherwise qualify for Priority Review. The Rare Pediatric Disease Priority Review Voucher program is designed to encourage development of new drugs and biologics for the prevention or treatment of rare pediatric diseases.

In order to support patients, Ultragenyx has launched UltraCare™, a support service that will provide ongoing support to patients and caregivers. UltraCare will help patients understand insurance coverage and assist in finding financial support for both medication and administration of medication. Dedicated in-house UltraCare Guides are available Monday through Friday from 9 a.m. to 8 p.m. Eastern Time at 888-756-8657 to assist patients and their families.

Kyowa Hakko Kirin, Kyowa Kirin International, a wholly owned subsidiary of Kyowa Hakko Kirin, and Ultragenyx have been collaborating in the development and commercialization of Crysvita globally, based on the collaboration and license agreement between Kyowa Hakko Kirin and Ultragenyx.

Efficacy Results in Clinical Studies

For the pediatric XLH population, the FDA approval is supported by 64-week data from Study CL201, a randomized, open-label study in 52 patients ages 5 to 12, which showed that treatment with Crysvita improved rickets, increased serum phosphorus levels, decreased serum alkaline phosphatase activity, and increased growth. The indication is also supported by 40-week data from Study CL205, an open-label study in 13 patients ages 1 to 4. In these patients, Crysvita improved rickets and lower-limb deformity, increased serum phosphorus levels and decreased serum alkaline phosphatase activity.

For the adult XLH indication, the FDA approval is supported by 24-week data from Study CL303, a randomized, double-blind, placebo-controlled study in 134 adult XLH patients. Crysvita treatment resulted in a higher proportion of patients achieving serum phosphorus levels above the lower limit of normal, and a higher rate of complete healing of active fractures and pseudofractures, compared to placebo. The adult indication is also supported by data from

the 48-week, open-label, single-arm bone biopsy study in 14 adult XLH patients, which showed healing of osteomalacia as demonstrated by decreases in osteoid volume/bone volume, osteoid thickness and mineralization lag time.

About Crysvita

Crysvita is a recombinant fully human monoclonal IgG1 antibody, discovered by Kyowa Hakko Kirin, against the phosphaturic hormone fibroblast growth factor 23 (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 is caused by excessive levels and activity of FGF23. Crysvita is designed to bind to and thereby inhibit the biological activity of FGF23. By blocking excess FGF23 in patients, Crysvita is intended to increase phosphate reabsorption from the kidney and increase the production of active vitamin D, which enhances intestinal absorption of phosphate and calcium.

INDICATION (IN THE U.S.)

Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients one year of age and older.

IMPORTANT SAFETY INFORMATION

Crysvita should not be taken if:

- An oral phosphate supplement and a specific form of vitamin D supplement are taken
- Phosphorus levels from a blood sample are within or above the normal range for age
- Kidney problems are present

What is the most important information to know about Crysvita?

- Some patients developed allergic reactions (rash and hives) while taking Crysvita. Doctors will monitor for symptoms of an allergic reaction while Crysvita is taken.
- High levels of phosphorus in the blood have been reported in some patients taking Crysvita. This may be related to a risk of high calcium levels in the kidneys. Doctors will collect samples to monitor levels.
- Administration of Crysvita may result in reactions at the injection site, such as hives, reddening of the skin, rash, swelling, bruising, pain, severe itching of the skin, and collection of blood outside of a blood vessel (hematoma).

What are the possible side effects of Crysvita?

- The most common adverse reactions that were seen in children with XLH are:
    - Headache
    - Injection site reaction
    - Vomiting

- Fever
- Pain in arms and legs
- Decreased vitamin D levels
- Rash
- Toothache
- Muscle pain
- Tooth infection
- Dizziness

- The most common adverse reactions that were seen in adults with XLH are:
  - Back pain
  - Headache
  - Tooth infection
  - Restless leg syndrome
  - Decreased vitamin D levels
  - Dizziness
  - Constipation
  - Phosphorus levels increased in the blood

- Narrowing of the spaces within the spine is common in adults with XLH and pressure on the spinal cord has been reported in adults taking Crysvita. It is not known if taking Crysvita worsens the narrowing of the spaces within the spine or the pressure on the spinal cord.

Before taking Crysvita, doctors should be informed about all medical conditions, including if:

- One is pregnant, thinks she may be pregnant, or plans to become pregnant. There is not enough experience to know if Crysvita may harm an unborn baby. Report pregnancies to the Ultragenyx Adverse Event reporting line at 1-888-756-8657.
- One is breastfeeding or plans to breastfeed. There is not enough experience to know if Crysvita passes into breast milk. Women should talk with their doctors about the best way to feed their babies while taking Crysvita.

While taking Crysvita, doctors should be informed if one experiences:

- An allergic reaction such as rash or hives
- A rash, swelling, bruising or other reaction at the injection site
- New or worsening restless leg syndrome

These are not all the possible side effects of Crysvita. Doctors should be contacted for medical advice about side effects.

Side effects may be reported to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. Side effects may also be reported to Ultragenyx at 1-888-756-8657.

Please see full Prescribing Information for additional Important Safety Information.

About Ultragenyx

Ultragenyx is a biopharmaceutical company committed to bringing to patients novel therapies 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 approved and investigational therapies 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 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.

Kyowa Kirin International PLC is a wholly owned 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. Kyowa Kirin International is headquartered in Scotland.

You can learn more about the business at: www.kyowa-kirin.com.

Forward-Looking Statements

Except for the historical information contained herein, the matters set forth in this press release, including statements relating to Ultragenyx's plans or expectations regarding the availability of Crysvita, 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 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 Ultragenyx in general, see Ultragenyx's Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 21, 2018, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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