Kyowa Kirin and Ultragenyx Announce Crysvita® (burosumab) Receives Conditional Marketing Authorisation in Europe for the Treatment of X–Linked Hypophosphatemia in Children

Crysvita is the First Treatment for XLH that Targets the Underlying Cause of the Disease

Crysvita Acknowledged by European Medicines Agency as an Outstanding Contribution to Public Health

Tokyo, Japan, London, UK and Novato, CA. – February 23, 2018: Kyowa Hakko Kirin Co. Ltd, (Kyowa Hakko Kirin), Kyowa Kirin International PLC (Kyowa Kirin International) and Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE: Ultragenyx) today announce that Crysvita (burosumab) has received a positive European Commission decision granting a conditional marketing authorisation to Kyowa Kirin for the treatment of X-linked hypophosphatemia (XLH) with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons. XLH is a rare, chronic progressive musculoskeletal disorder that affects children and adults.

This is the first regulatory approval globally for Crysvita, an anti-FGF23 fully human monoclonal antibody that is the first treatment to target the underlying pathophysiology of XLH. The European Medicines Agency recently acknowledged Crysvita as an outstanding contribution to public health and a significant improvement in the endocrinology therapeutic area.

The European Marketing Authorisation is valid in the 28 countries of the European Union and in Norway, Iceland and Liechtenstein. The first commercial launch of Crysvita is expected to take place in Germany in the second quarter of 2018, followed by other European countries.

“Today’s news brings hope to people affected by XLH in Europe, and it’s exciting that Europe is the first global regulatory approval for Crysvita,” said Dr Tom Stratford, President and Chief Executive Officer of Kyowa Kirin International. “We will now focus our efforts on working with health authorities to ensure patient access in European countries. We will also continue our work with the healthcare and patient community to further develop our understanding of the real-world experience of people affected by XLH. This will help to ensure appropriate patient identification and diagnosis and improve standards of care for this rare condition.”

“Throughout our 20-year journey of scientific discovery with XLH and burosumab, we have been guided by the needs of the people affected by this debilitating condition,” said Mitsuo Satoh, Ph.D., Executive Officer, Vice President Head of R&D Division of Kyowa Hakko Kirin. “We look forward to continuing our scientific endeavours in nephrology and bone metabolism to help improve outcomes for these patients.”

“XLH is extremely debilitating to patients and this authorisation in Europe provides children with the first treatment option that addresses the excess FGF23 activity in XLH,” said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. “Through this authorisation and our work throughout the rest of the world we are committed to bringing Crysvita to all patients with XLH who could benefit from the therapy.”

The authorisation follows a positive opinion adopted on 15 December 2017 by the European Committee for Medicinal Products for Human Use to recommend conditional approval of Crysvita for the treatment of X-linked hypophosphatemia (XLH) with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons. The CHMP recommendation is based on data from clinical trials of the antibody for paediatric XLH.

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

About X-Linked Hypophosphatemia (XLH)

XLH is a rare, chronic progressive musculoskeletal disorder characterised by renal phosphate wasting caused by excess FGF23 production, and is inherited as an X-linked dominant trait affecting both males and females. XLH is first seen in infants and also affects adults.

In children, XLH causes skeletal disease, leading to lower-extremity deformity and diminished height.

The conventional treatment of XLH consists of multiple daily doses of phosphate and active vitamin D to counteract the excess effects of FGF23 but does not correct the underlying disease.

About Crysvita

Crysvita (burosumab) 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. Crysvita is being developed to treat XLH and tumour-induced osteomalacia (TIO), diseases characterised by excess levels of FGF23. Phosphate wasting in XLH and TIO is caused by excessive levels and activity of FGF23. Crystiva is designed to bind to and thereby inhibit the biological activity of FGF23. By blocking excess FGF23 in patients with XLH and TIO, Crysvita is intended to increase phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

In the United States, the U.S. Food and Drug Administration (FDA) is currently reviewing the Biologics License Application for Crysvita to treat paediatric and adult patients with XLH, and has set a Prescription Drug User Fee Act (PDUFA) action date of April 17, 2018.

A clinical programme studying Crysvita in adults and paediatric patients with XLH is ongoing. Crysvita 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 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.

About Ultragenyx

Ultragenyx is a biopharmaceutical company committed to bringing to patients 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.

Forward-Looking Statements

Except for the historical information contained herein, the matters set forth in this press release, including statements relating to Ultragenyx's expectations regarding future regulatory

interactions, the potential timing and success of filings for regulatory approvals, potential indications for its product candidates and plans for its clinical programs and clinical 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 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 Quarterly 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.