

News release

Kyowa Kirin Announces Crysvita[®] Now Reimbursed for Self-Injection in Japan

Tokyo, Japan, December 4, 2020 – Kyowa Kirin Co., Ltd. (TSE: 4151, President and CEO: Masashi Miyamoto, "Kyowa Kirin") announced today that Crysvita[®] (burosumab) is now available to be reimbursed by National Health Insurance (NHI) as a self-injection formulation for the treatment of FGF23-related hypophosphatemic rickets and osteomalacia in Japan, December 1, 2020.

Crysvita is a recombinant fully human monoclonal IgG1 antibody, discovered by Kyowa Kirin, and is the first drug that directly targets fibroblast growth factor 23 (FGF23), a "phosphaturic" hormone. FGF23 reduces serum levels of phosphorus by regulating phosphate excretion and vitamin D activation in the kidney. Crysvita has been developed to treat FGF23-related hypophosphatemic diseases, such as X-linked hypophosphatemia (XLH) and tumor-induced osteomalacia (TIO). In September 2019, Crysvita was approved for the treatment of FGF23-related hypophosphatemic rickets and osteomalacia, and was launched in December 2019 in Japan.

"I am pleased that reimbursement means that more patients may now be able to access this treatment option," said Hiroshi Sugitani, Managing Executive Officer, Vice President, Head of Sales & Marketing Division, Kyowa Kirin. "We hope the availability of this treatment option will be a valuable addition for healthcare professionals in Japan and their patients."

Kyowa Kirin and Ultragenyx Pharmaceutical Inc. (Ultragenyx) have been collaborating in the development and commercialization of burosumab globally based on a license agreement between the two companies.

The Kyowa 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 FGF23-related Hypophosphatemic Rickets and Osteomalacia

FGF23-related hypophosphatemic rickets and osteomalacia is an inclusive term for diseases caused by excessive actions of FGF23, which leads to impaired phosphate reabsorption in the

renal proximal tubules. In Japan, the disease corresponds to vitamin D resistant rickets and osteomalacia (Intractable Diseases) and primary hypophosphataemic rickets and vitamin D resistant osteomalacia (Specific Pediatric Chronic Diseases). The term also encompasses diseases, such as XLH, TIO and epidermal nevus syndrome (ENS). These diseases are rare, and characterized by skeletal disorders associated with renal phosphate wasting.

The excess production of FGF23 in XLH patients is caused by inactivating mutations in the *PHEX* (phosphate-regulating gene with homologies to endopeptidases on the X chromosome) gene while ADHR (autosomal dominant hypophosphatemic rickets) patients are reported to be the result of FGF23 gene mutations. Other relevant diseases of FGF23-related hypophosphatemic rickets and osteomalacia are TIO, in which excess FGF23 production is caused by tumors and ENS, in which it is caused by skin lesions.

About Crysvida (burosumab)

Crysvida (burosumab) was discovered by Kyowa Kirin and is a recombinant fully human monoclonal IgG1 antibody against the phosphaturic hormone fibroblast growth factor 23 (FGF23). FGF23 is a hormone that reduces serum levels of phosphate by regulating phosphate excretion and active vitamin D production by the kidney. Phosphate wasting and resulting hypophosphataemia in X-linked hypophosphataemia (XLH) is caused by excessive levels and activity of FGF23. Crysvida is designed to bind to, and thereby inhibit, the biological activity of FGF23. By blocking excess FGF23 in patients, Crysvida is designed to increase phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

In Japan, Crysvida received approval from Japan's Ministry of Health, Labour and Welfare (MHLW) for the treatment of FGF23-related hypophosphatemic rickets and osteomalacia in September 2019.

In Europe, the European Commission (EC) granted a conditional marketing authorization for Crysvida for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and in adolescents with growing skeletons in 2018, and for use in older adolescents and adults with XLH in September 2020. In January 2020, Swissmedic approved Crysvida for the treatment of adults, adolescents and children (one year of age and older) with XLH.

In North America, Crysvida received approval from the US Food and Drug Administration (FDA) and Health Canada for pediatric and adult use in 2018, and received approval from the FDA for the treatment of fibroblast growth factor 23 (FGF23)-related hypophosphatemia in TIO associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older in June 2020.

About Kyowa Kirin

Kyowa Kirin commits to innovative drug discovery driven by state-of-the-art technologies. The company focuses on creating new values in the four therapeutic areas: nephrology, oncology, immunology/allergy and neurology. Under the Kyowa Kirin brand, employees from 40 group companies across North America, EMEA and Asia/Oceania unite to champion the interests of patients and their caregivers in discovering solutions wherever there are unmet medical needs. You can learn more about the business of Kyowa Kirin at <https://www.kyowakirin.com>.

About Ultragenyx Pharmaceutical Inc.

Ultragenyx (NASDAQ: RARE) is a biopharmaceutical company committed to bringing to patients novel products for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are no approved therapies treating the underlying disease.

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.

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