

News release

Long-term CRYSVITA® ▼ (burosumab) treatment reduces the burden of disease in adults with X-Linked Hypophosphataemia (XLH), a rare genetic metabolic bone disease

Extended CRYSVITA therapy significantly improves pain, stiffness, fatigue and physical and ambulatory function compared to baseline after 96 weeks

TOKYO, Japan, 27 September 2021 – Kyowa Kirin Co., Ltd. (TSE:4151, Kyowa Kirin) today announced the publication of new data highlighting the sustained benefits of treatment with CRYSVITA® (burosumab) in adults with X-linked hypophosphataemia (XLH), a rare genetic metabolic bone disease. The data show that adults with XLH experience substantial pain, stiffness, fatigue and impairment in physical and ambulatory function. Treatment with CRYSVITA was associated with a significant improvement from baseline after 96 weeks.¹

The data are from a randomised, double-blind, placebo-controlled, phase 3 study with an open-label extension to assess the efficacy and safety of CRYSVITA in adults with XLH.² The study met its primary endpoint, showing a statistically significant effect in increasing serum phosphorus concentrations at 24 weeks, compared to placebo.³ After 24 weeks, all patients were switched to CRYSVITA treatment and data was collected on metabolic and biochemical markers, patient reported outcomes (PROs) and measures of mobility up to 96 weeks. This new publication focuses on the results from the PRO analysis and mobility scores.¹

At week 96, the study showed statistically significant improvements in PROs, including the Western Ontario and the McMaster Universities Osteoarthritis Index (WOMAC), Brief Pain Inventory–Short Form (BPI-SF) and Brief Fatigue Inventory (BFI), compared to baseline.¹ Statistically significant improvements in ambulatory function, measured by the 6-minute walk test (6MWT), were also seen at 96 weeks compared to baseline.¹ Data previously published at 48 weeks also showed improvements in some PROs, including stiffness and pain, as well as fracture healing.³

Lead author Pr Karine Briot, Hôpital Cochin, Paris, France said: “The study highlights the many physical challenges faced by adult patients with XLH, including pain, stiffness, fatigue and difficulty walking or physical function. Burosumab treatment has previously been shown to improve phosphate homeostasis in adult XLH patients, compared to placebo. This new analysis suggests that, despite the long-term complications and physical impairment associated with XLH in adults, treatment with burosumab can also improve the physical function and quality of life of adults with XLH over the longer term.”

Tomohiro Sudo, Executive Officer, Head of Global Product Strategy Department of Kyowa Kirin, said: “Kyowa Kirin is committed to improving the lives of people with XLH and their families. One of our areas of focus is to

generate new data that improve our understanding of how best to manage and treat XLH. These important new data highlight the many physical challenges that people living with XLH face every day, how their needs could be better met and how Kyowa Kirin is delivering on its purpose, to make people smile.”

The data were published today in the *BMJ* journal *RMD Open, Rheumatic and Musculoskeletal Diseases*.¹ CRYSVITA is licensed in Europe for the treatment of XLH in children and adolescents aged 1 to 17 years with radiographic evidence of bone disease, and in adults.⁴

▼ This medicinal product is subject to additional monitoring.

About X-linked hypophosphataemia

X-linked hypophosphataemia (XLH) is a rare, genetic disease that causes abnormalities in the bones, muscles, and joints.^{5,6} XLH is not life-threatening, but its burden is life-long and progressive, and it may reduce a person’s quality of life.⁷

People with XLH have a genetic defect on the X-chromosome, which causes an excessive loss of phosphate through the urine and poor absorption from the gut due to excess of a hormone known as fibroblast growth factor-23 (FGF23), resulting in chronically low levels of phosphate in the blood.^{7,8} Phosphate is a key mineral needed for maintaining the body’s energy levels, muscle function, and the formation of healthy bones and teeth.^{9,10} While there is no cure for XLH, therapies aimed at helping to restore and maintain phosphate to normal levels within the body may help to improve the progression of disease symptoms.²

XLH is the most common form of hereditary rickets.¹¹ It can sometimes appear in individuals with no family history of the disease but is usually passed down from a parent who carries the defective gene.¹²

About CRYSVITA® (burosumab)

[CRYSVITA \(burosumab\)](#) was created and developed 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 excess 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.

CRYSVITA has been available for clinical use since 2018. The first approval came from the European Commission, that granted a conditional marketing authorisation for CRYSVITA for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing

skeletons. In 2020, this authorisation was subsequently expanded to include older adolescents and adults.⁴

CRYSVITA is approved by the US Food and Drug Administration (FDA) for patients with XLH aged 6 months and older and by Health Canada for patients with XLH aged one year and older.^{13,14}

In 2019, CRYSVITA received approval from Japan's Ministry of Health, Labour and Welfare for the treatment of FGF23-related hypophosphataemic rickets and osteomalacia. In 2020, CRYSVITA was reimbursed by National Health Insurance (NHI) in Japan as a self-injection presentation for the treatment of FGF23-related hypophosphataemic rickets and osteomalacia.

In January 2020, Swissmedic approved CRYSVITA for the treatment of adults, adolescents and children (one year of age and older) with XLH.¹⁵

In June 2020, the U.S. Food and Drug Administration (FDA) approved CRYSVITA for patients aged two and older with tumour-induced osteomalacia (TIO), a rare disease that is characterised by the development of tumours that cause weakened and softened bones.¹⁶

Kyowa Kirin and Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE: Ultragenyx) have been collaborating in the development and commercialisation of CRYSVITA globally, based on the collaboration and licence agreement between Kyowa Kirin and Ultragenyx.

About Kyowa Kirin

Kyowa Kirin strives to create and deliver novel medicines with life-changing value. As a Japan-based Global Specialty Pharmaceutical Company with a more than 70-year heritage, the company applies cutting-edge science including an expertise in antibody research and engineering, to address the needs of patients and society across multiple therapeutic areas including Nephrology, Oncology, Immunology/Allergy and Neurology. Across our four regions – Japan, Asia Pacific, North America and EMEA/International – we focus on our purpose, to make people smile, and are united by our shared values of commitment to life, teamwork/Wa, innovation, and integrity. You can learn more about the business of Kyowa Kirin at: <https://www.kyowakirin.com/>

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