News release

Kyowa Kirin announces the presentations about Crysvita® (burosumab) at American Society for Bone and Mineral Research (ASBMR) 2021 Annual Meeting

TOKYO, Japan, 1 October 2021 – Kyowa Kirin Co., Ltd. (TSE: 4151, Kyowa Kirin) today announced that new data highlighting Crysvita® (burosumab-twza) for the treatment of X-linked hypophosphatemia (XLH) will be presented at the American Society for Bone and Mineral Research (ASBMR) 2021 Annual Meeting by Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), with which Kyowa Kirin has been collaborating in the development and commercialization of Crysvita globally. The meeting will take place October 1-4 in-person in San Diego with programming also virtually accessible in real-time.

Details for the presentations are as follows:

Oral Presentations

- Neurological and Psychiatric Manifestations of X-Linked Hypophosphatemia in a Longitudinal Cohort Study: XLH Disease Monitoring Program (XLH-DMP)
  - Presentation #1019: Friday, October 1, 2:15-2:30 p.m. PT
  - Presenter: Suzanne Jan de Beur, M.D.

- Burosumab Improves Lower Limb Alignment in Children with X-Linked Hypophosphatemia
  - Presentation #1020: Friday, October 1, 2:30-2:45 p.m. PT
  - Presenter: David Frumberg, M.D.

Poster Presentations

- Patient Perspective: XLH Requires Whole-Body, Whole-Life, Whole-Family Care
  - SAT-268: Saturday, October 2, 1:00-3:00 p.m. PT

- Adolescents with X-linked hypophosphatemia (XLH): first year of real-world data from the XLH Disease Monitoring Program (DMP)
  - SAT-269: Saturday, October 2, 1:00-3:00 p.m. PT

- Rarediseasegenes.com/phex: A comprehensive locus specific database of PHEX gene variants associated with X-linked hypophosphatemia vastly increases the number of known variants.
    - SUN-274: Sunday, October 3, 1:00-3:00 p.m. PT

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 X-linked hypophosphatemia

X-linked hypophosphatemia (XLH) is a rare, genetic disease that causes abnormalities in the bones, muscles, and joints. XLH is not life-threatening, but its burden is life-long and progressive, and it may reduce a person's quality of life.

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. Phosphate is a key mineral needed for maintaining the body's energy levels, muscle function, and the formation of healthy bones and teeth. 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.

XLH is the most common form of hereditary rickets. 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.

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 hypophosphatemia in X-linked hypophosphatemia (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 in February 2018, that granted a conditional marketing authorization 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 Octocer 2020, this authorization was subsequently expanded to include older adolescents and adults. In July 2021, CRYSVITA was approved for the option of self-administration in EU for the treatment of XLH.

CRYSVITA was approved by the US Food and Drug Administration (FDA) in April 2018 for patients with XLH aged one year and older and by Health Canada in December 2018 for patients with XLH aged one year and older. These authorizations have now been expanded to include 6-12 months of age.

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

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

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

Crysvita U.S. INDICATION

Crysvita® (burosumab-twza) is a fibroblast growth factor 23 (FGF23)-blocking antibody indicated for the treatment of:

- X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.
- FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adult and pediatric patients 2 years of age and older.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS

- With oral phosphate and/or active vitamin D analogs (e.g., calcitriol, paricalcitol, doxercalciferol, calcifediol).
- When serum phosphorus is within or above the normal range for age.
- In patients with severe renal impairment or end stage renal disease.

WARNINGS AND PRECAUTIONS
Hypersensitivity

- Discontinue Crysvita if serious hypersensitivity reactions occur and initiate appropriate medical treatment.

Hyperphosphatemia and Risk of Nephrocalcinosis

- For patients already taking Crysvita, dose interruption and/or dose reduction may be required based on a patient's serum phosphorus levels.
- Patients with TIO who undergo treatment of the underlying tumor should have dosing interrupted and adjusted to prevent hyperphosphatemia.

Injection Site Reactions

- Discontinue Crysvita if severe injection site reactions occur and administer appropriate medical treatment.

ADVERSE REACTIONS
Pediatric XLH Patients

- Adverse reactions reported in 10% or more of Crysvita-treated pediatric XLH patients across all studies are: pyrexia, injection site reaction, cough, vomiting, pain in

extremity, headache, tooth abscess, dental caries, diarrhea, vitamin D decreased, toothache, constipation, myalgia, rash, dizziness, and nausea.
- Post-marketing experience reported in pediatric XLH patients receiving Crysvita – blood phosphorus increased.

Adult XLH Patients

- Adverse reactions reported in more than 5% of Crysvita-treated adult XLH patients and in at least 2 patients more than placebo in one study are: back pain, headache, tooth infection, restless legs syndrome, vitamin D decreased, dizziness, constipation, muscle spasms, and blood phosphorus increased.
- Spinal stenosis is prevalent in adults with XLH, and spinal cord compression has been reported. It is unknown if Crysvita therapy exacerbates spinal stenosis or spinal cord compression.

Adult TIO Patients

- Adverse reactions reported in more than 10% of Crysvita-treated adult TIO patients in two studies are: tooth abscess, muscle spasms, dizziness, constipation, injection site reaction, rash, and headache.

USE IN SPECIFIC POPULATIONS

- There are no available data on Crysvita use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Serum phosphorus levels should be monitored throughout pregnancy. Report pregnancies to the Kyowa Kirin, Inc. Adverse Event reporting line at 1-888-756-8657.
- There is no information regarding the presence of Crysvita in human milk or the effects of Crysvita on milk production or the breastfed infant.

PATIENT COUNSELING INFORMATION

- Advise patients not to use any oral phosphate and/or active vitamin D analog products.
- Instruct patients to contact their physician if hypersensitivity reactions, injection site reactions, and restless leg syndrome induction or worsening of symptoms occur.

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

Please see full Prescribing Information for a complete discussion of the risks associated with CRYSVITA.