

Kyowa Hakko Kirin Submits Application for Approval of Burosumab for FGF23-related Hypophosphatemic Rickets and Osteomalacia in Japan

Tokyo, Japan— January 7, 2019 —Kyowa Hakko Kirin Co., Ltd. (Tokyo: 4151, President and COO: Masashi Miyamoto, "Kyowa Hakko Kirin") today announced that it has filed an application for manufacturing and marketing approval with Japan's Ministry of Health, Labor and Welfare (MHLW) for burosumab (code name: KRN23) to treat FGF23-related hypophosphatemic rickets and osteomalacia.

Burosumab is a recombinant fully human monoclonal IgG1 antibody, discovered by Kyowa Hakko Kirin, against the phosphaturic hormone fibroblast growth factor 23 (FGF23). FGF23 reduces serum levels of phosphorus and active vitamin D by regulating phosphate excretion and active vitamin D production by the kidney. Burosumab has been developed to treat FGF23-related hypophosphatemic disease such as X-Linked Hypophosphatemia (XLH) and tumor-induced osteomalacia (TIO)/epidermal nevus Syndrome (ENS).

Phosphate wasting in FGF23-related hypophosphatemic rickets and osteomalacia is caused by excessive levels and activity of FGF23. Burosumab is designed to bind to, and thereby inhibit, the biological activity of FGF23. By blocking excess FGF23 in patients, burosumab increases phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

“Burosumab is the culmination of Kyowa Hakko Kirin’s research activity into FGF23-related hypophosphatemic disease,” said Mitsuo Satoh, Ph.D., Executive Officer, Vice President Head of Research and Development Division of Kyowa Hakko Kirin. “I believe burosumab has the potential to be an effective treatment option for patients with FGF23-related hypophosphatemic rickets and osteomalacia in Japan and we will keep working to provide this advance in therapy for patients as soon as possible.”

Burosumab received orphan drug designation by the Ministry of Health, Labour and Welfare in Japan for FGF23-related hypophosphatemic rickets and osteomalacia. Kyowa Hakko Kirin expects to receive feedback from MHLW regarding manufacturing and marketing approval for burosumab around September, 2019.

Kyowa Hakko Kirin, Kyowa Kirin International PLC., a member of Kyowa Hakko Kirin group, and Ultragenyx Pharmaceutical Inc. (Ultragenyx) have been collaborating in the development and commercialization of burosumab globally based on a collaboration and license agreement between Kyowa Hakko Kirin and Ultragenyx.

About XLH

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 delayed growth and decreased height. Adults with XLH have an increased risk of fractures, softening of the bones, and stiffness.

About TIO/ENS

TIO, and a skin lesion variant, epidermal nevus syndrome (ENS)-associated osteomalacia, are caused by typically benign tumors or lesions that produce excess levels of FGF23, causing phosphate wasting in the urine that leads to severe hypophosphatemia, osteomalacia, muscle weakness, fatigue, bone pain, and fractures. The symptoms rapidly resolve if the causal tumors or lesion can be resected; however, there are cases in which resection is not feasible or recurrence of the tumor occurs after resection. In patients for whom the tumor or lesion is inoperable, the current treatment consists of oral phosphate and/or vitamin D replacement. Efficacy of this treatment is often limited, as it does not treat the underlying disease and its benefits must be balanced with monitoring for potential risks such as nephrocalcinosis, hypercalciuria, and hyperparathyroidism.

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 centered 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 realize its vision of becoming a Japan-based global specialty pharmaceutical company that contributes to the health and wellbeing of people around the world.

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

About Ultragenyx Pharmaceutical Inc.

Ultragenyx 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.

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.