Kyowa Hakko Kirin and Kyowa Kirin International Announce Regulatory Updates for Burosumab in the US and EU.

Tokyo, Japan and London, UK — July 28, 2017 — Kyowa Hakko Kirin Co., Ltd. (Kyowa Hakko Kirin) and Kyowa Kirin International PLC (Kyowa Kirin International), a wholly owned subsidiary of Kyowa Hakko Kirin, today announced the biologics license application (BLA) submission plan in August for burosumab in the US and an update on the ongoing regulatory process in the EU. Burosumab is an investigational recombinant fully human monoclonal IgG_1 antibody and being developed by Kyowa Hakko Kirin, Kyowa Kirin International and Ultragenyx Pharmaceutical (NASDAQ: RARE).

1. **US: Submission of a BLA for burosumab for the treatment of pediatric and adult XLH patients planned in August 2017.**
   In June 2017, the FDA agreed that the BLA could be submitted based on available clinical data and confirmed that both pediatric and adult indications would be included in the review. Specifically for pediatric patients the filing will include the 64-week data from our Phase 2 study in 5-12 year olds and 24-week data from our Phase 2 study in 1-4 year olds. The FDA confirmed that data from the ongoing pediatric Phase 3 study would not be required for the BLA filing. To support the adult indication, the submission will include the 24-week placebo-controlled data from the adult Phase 3 study. Additionally, FDA agreed to accept available bone biopsy data from the 48 week open label bone quality study in adults as supportive evidence.
2. **US: Burosumab designated a drug for a "rare pediatric disease".**
   The FDA's Office of Orphan Drug Development (OOPD) has recently designated burosumab for the treatment of X-linked hypophosphatemia (XLH) as a drug for a "rare pediatric disease". Under FDA's Rare Pediatric Disease Priority Review Voucher program, companies who receive an approval for a new drug application or BLA for a rare pediatric disease may be eligible to receive a voucher for a Priority Review of a subsequent marketing application for a different product. The Priority Review Voucher may be used by the company or sold to a third party.
3. **EU: Conditional Marketing Authorization Application (MAA) to be focused on pediatric indication.**
   Conditional MAA in the EU was filed in December 2016 without recently obtained adult Phase 3 data for pediatric and adult indications. To ensure the expeditious availability of burosumab for pediatric XLH patients in Europe and to avoid any potential delays in the review procedure due to the large amount of recent data from the adult XLH Phase 3 study to be filed, Kyowa Hakko Kirin and Kyowa Kirin International have decided to separate the adult and pediatric indications. A filing for the adult indication is planned after a decision is first reached on the pediatric indication.

Kyowa Kirin and Ultragenyx entered into a collaboration and license agreement in August 2013 to develop and commercialise burosumab. In May 2017, a wholly-owned subsidiary of Kyowa Kirin and Ultragenyx entered into an agreement that Ultragenyx was granted the

right to commercialise burosumab in Turkey. Kyowa Kirin has the option to take over commercialisation efforts after a certain minimum period.

The Kyowa Hakko 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 burosumab

Burosumab is an investigational recombinant fully human monoclonal IgG1 antibody, discovered by Kyowa Hakko Kirin, against the phosphaturic hormone fibroblast growth factor 23 (FGF23). It is being developed by Ultragenyx and Kyowa Hakko Kirin to treat XLH and TIO, diseases characterised by excess activity of 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. Phosphate wasting in XLH and TIO is caused by excessive levels and activity of FGF23. Burosumab is designed to bind to, and thereby inhibit, the excessive biological activity of FGF23. By blocking excess FGF23 in patients with XLH and TIO, burosumab is intended to increase phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

A Phase 3 programme studying burosumab in adults and Phase 2 and Phase 3 studies in paediatric patients with XLH are ongoing. Burosumab is also being developed for tumour-induced osteomalacia (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 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.

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.