KYOWA KIRIN

Company / Media Contact:
Debbie Johnston
Spreng Thomson Ltd.
(For Kyowa Kirin
International PLC)
+44 (0)141 548 5191
Mobile: +44 (0)7532 183811

FIRST EARLY ACCESS PROGRAMME INITIATED FOR KYOWA KIRIN INTERNATIONAL'S INVESTIGATIONAL TREATMENT FOR X-LINKED HYPOPHOSPHATEMIA (XLH)

- *Kyowa Kirin International's burosumab (KRN23) is an investigational recombinant fully human monoclonal IgG1 being evaluated by the European Medicines Agency as the first potential treatment for XLH*
- *Germany's Paul-Ehrlich-Institute, the Federal Institute for Vaccines and Biomedicines has confirmed the notification for compassionate use of burosumab*

Galashiels, Scotland — 24 July, 2017 — Kyowa Kirin International PLC, a wholly owned subsidiary of Kyowa Hakko Kirin Co., Ltd. (Kyowa Hakko Kirin) today announces Germany's Federal Institute for Vaccines and Biomedicines has confirmed the notification through the Ordinance on Medicinal Products for Compassionate Use (Arzneimittel-Härtefall-Verordnung, AMHV) to make burosumab available to eligible paediatric patients with X-Linked Hypophosphatemia* (XLH). Burosumab is an investigational treatment for XLH.[1] This notification means that eligible paediatric XLH patients in Germany can now have access to burosumab. This is the first Early Access Programme to be launched for XLH worldwide.

The Ordinance on Medicinal Products for Compassionate Use aims to give people with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation, and has only been granted to a limited number of products since its inception in 2014.[2]

XLH is a rare, genetic bone disorder characterised by urinary phosphate wasting due to excess production of FGF23.[3] Children with XLH may have rickets, progressive bowing of the leg, osteomalacia, bone pain, waddling gait, short stature, gross motor impairment, muscle weakness, frequent/poorly healing pseudofractures, spinal stenosis, enthesopathy and osteoarthritis.[4,5,6] It is estimated that prevalence of XLH in children is approximately one in every 20,000.[7]

"This notification is an important step for burosumab and we are proud to have entered into the voluntary Ordinanace on Medicinal Products for Compassionate Use" said Dr. Tom Stratford, President and CEO of Kyowa Kirin International.

**XLH is also known as "Phosphatdiabetes" in Germany.*

KYOWA KIRIN

Notes to Editors

About X-Linked Hypophosphatemia (XLH)
XLH is the most common heritable form of rickets (the softening and weakening of bones)[3] that is inherited as an X-linked dominant trait affecting both males and females.

Most paediatric patients and some adult patients are managed using oral phosphate replacement and active vitamin D (calcitriol) therapy, which requires multiple divided doses each day and monitoring for potential risks such as nephrocalcinosis, hypercalciuria, and hyperparathyroidism.[8]

About KRN23
KRN23 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 Kyowa Hakko Kirin and Ultragenyx to treat XLH and tumour-induced osteomalacia (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. KRN23 is designed to bind to and thereby inhibit the excessive biological activity of FGF23. By blocking excess FGF23 in patients with XLH and TIO, KRN23 is intended to increase phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

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 centred 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 realise its vision of becoming a Japan-based global specialty pharmaceutical company that contributes to the health and comfort of people around the world.

Kyowa Kirin International PLC is a 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.

For more information on Kyowa Kirin please visit: www.kyowa-kirin.com

KYOWA KIRIN

References

[1] A Study of KRN23 for X-linked hypophosphatemia. Available at: https://clinicaltrials.gov/ct2/show/NCT00830674?cond=XLH&draw=1&rank=7 Last accessed July 2017.

[2] Paul-Ehrlich-Institut. Available here: http://www.pei.de/EN/information/license-applicants/clinical-trial-authorisation/compassionate-use/compassionate-use- Last accessed July 2017.

3 Carpenter TO et al. A clinician's guide to X-linked hypophosphatemia. J Bone Miner Res. 2011;26:1381–1388. Available here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3157040/ Last accessed July 2017.

[4] Carpenter TO, Imel E, Ruppe M *et al.* Randomized trial of the anti-FGF23 antibody KRN23 in X-linked hypophosphatemia. *Journal of Clinical Investigation* 2014;124(4):1587-1597. Available here: https://www.ncbi.nlm.nih.gov/pubmed/24569459 Last accessed July 2017.

[5] Ming Yang H, Mao M, Yang F *et al*. Recombinant growth hormone therapy for X-linked Hypophosphatasemia in children. *Cochran Cystic Fibrosis and Genetic Disorders Group* 2005; doi:10.1002/14651858.CD004447.pub2.

[6] Beck-Nielsen et al. Incidence and prevalence of nutritional and hereditary rickets in southern Denmark Eur J Endocrinol 2009;160:491.

[7] Beck-Nielsen et al. Incidence and prevalence of nutritional and hereditary rickets in southern Denmark Eur J Endocrinol 2009;160:491.

[8] Lee J and Imel E. The changing face of hypophosphatemic disorders in the FGF-23 era. *Paediatric Endocrinology Review* 2013;10(2):367-379. Available here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4170520/ Last accessed July 2017.