



RESEARCH & DEVELOPMENT

Innovating therapeutic antibody drugs

Leaping forward as a global specialty pharmaceutical company

Kyowa Hakko Kirin Group provides high-quality products and services in the pharmaceutical and biochemical fields to contribute to the health and well-being of people around the world.

At the Group's core is Kyowa Hakko Kirin (KHK), a rapidly evolving global specialty pharmaceutical company (GSP). KHK develops innovative ethical drugs, driven by state-of-the-art

biotechnologies, focusing on nephrology, oncology, immunology/allergy, and neurology. Our clinical pipeline and product portfolio contain four main modalities: next-generation therapeutic antibodies, new types of small molecule drugs, nucleic acid drugs, and regenerative therapeutics.

Development of four major modalities

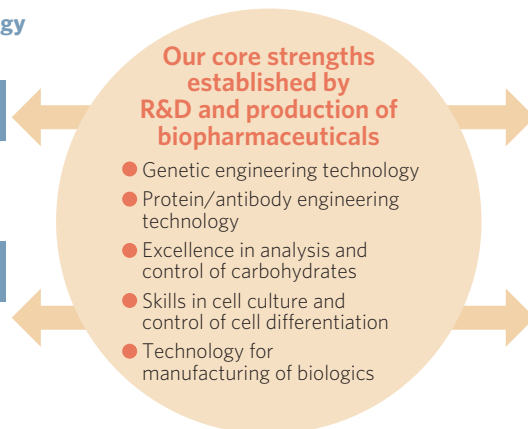
Further evolution of existing technology

Next-generation therapeutic antibodies

- Immuno activating antibody
- Cell/tissue homing antibody

New small molecule drugs

- Integrated approach with science of biologics
- Precise drug design and synthesis based on structural analysis of target molecule



Establishment of new technology

Nucleic acid drugs

- Nucleic acid function-enhancing technology
- DDS technology using lipid nanoparticles

Regenerative therapeutics

- iPS-T cell technology (collaboration with Kyoto University)
- Skills in stem cell culture and differentiation control



KRN23 (burosumab) for XLH: New treatment for a rare disease

A strategic product driving KHK's growth as a GSP is KRN23 (burosumab), which treats X-Linked hypophosphatemia (XLH), a bone disease caused by overexpression of phosphaturic hormone fibroblast growth factor 23 (FGF23).

In XLH, reduced serum levels of phosphorus and vitamin D prevent adequate mineralization of bone, leading to skeletal abnormalities, impaired growth, and extreme pain. XLH is a rare disease occurring in one out of 20,000 people in the world.

KRN23 is the first treatment to target the cause of the disease, by controlling excess FGF23. Current treatment offers only symptomatic relief by replacing phosphate and vitamin D, but requires frequent dosing and may cause renal calcification.

KHK discovered KRN23 — a recombinant fully human monoclonal IgG1 antibody — which effectively raises serum phosphorus level and maintains it within the normal range. Having proven safe and highly effective in clinical trials, KRN23 is attracting attention as a new treatment for this rare disease.

Collaboration for innovation

Since 2013 KHK has been progressing toward commercialization of KRN23 in collaboration with Ultragenyx, a U.S. biopharmaceutical company that focuses on treatment of rare genetic diseases.

In June 2016 the U.S. Food and Drug Administration (FDA) assigned breakthrough therapy designation to KRN23 for the treatment of XLH in pediatric patients, while in February 2018 the European Medicines Agency (EMA) granted Conditional Marketing Authorisation to KRN23 under the name Crysivita®. We also plan to introduce KRN23 to the U.S., Oceania, Japan, and other Asian nations following expanded regulatory approval.

Through the process of commercializing KRN23 we are building our marketing network and strengthening our foundation to leap ahead as a global specialty pharmaceutical company. We look forward to continued collaboration within and outside the Group as we fulfill our commitment to meeting society's needs through pharmaceutical innovation.



Adapted from Kyowa Hakko Kirin Group's FY2016–2020 Mid-term Business Plan