



Ultragenyx and Kyowa Kirin Announce Health Canada Approval of Crysvida™ (burosumab injection) for the Treatment of X-linked Hypophosphatemia (XLH) in Adults and Children

December 6, 2018

First Approved Treatment for XLH in Canada that Targets the Underlying Cause of this Rare, Hereditary, Lifelong Disease

NOVATO, Calif., TOKYO and LONDON, Dec. 06, 2018 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development of novel products for serious rare and ultra-rare genetic diseases, Kyowa Hakko Kirin Co. Ltd. (Kyowa Hakko Kirin), and Kyowa Kirin International PLC (Kyowa Kirin International) today announced that Crysvida™ (burosumab injection) has been approved by Health Canada for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients one year of age and older. The product is expected to be available for prescription to Canadian patients in early 2019. XLH is a rare, hereditary, lifelong disease.

"This approval of Crysvida offers Canadian patients living with XLH the first treatment option that targets the underlying cause of this rare and debilitating disease," said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. "Crysvida is now approved in the United States, Europe and Canada, all within one year, and Ultragenyx and Kyowa Kirin are pursuing regulatory filings in other countries to ensure that Crysvida is available to patients with XLH around the world as quickly as possible."

KYOWA KIRIN

"With this approval for Crysvida, now there is an entirely new option for XLH patients in Canada," said Toshifumi Mikayama, Ph.D., Director of the Board, and Senior Managing Executive Officer of Kyowa Hakko Kirin. "I am pleased that Crysvida will be able to make a major contribution to improving the lives of XLH patients in Canada and we are committed to working with those affected by this hereditary and lifelong disease in the world."

"Burosumab is the first treatment to address the fundamental problem in this disease – renal phosphate wasting," said Leanne Ward, MD, a Professor of Pediatrics at the University of Ottawa, where she holds a Research Chair in Pediatric Bone Health. "With this therapy, administered every 2 to 4 weeks subcutaneously, we see sustained improvements in phosphate metabolism and skeletal mineralization. Additional efforts are now underway to understand the longer-term benefits and side effects."

"Burosumab is a most welcome addition to the treatment options for XLH - a genetically transmitted form of rickets. This treatment has been shown to heal rickets in children and heal fractures and reduce stiffness in adult XLH patients, and is a breakthrough in the treatment of this disabling condition," says Dr. Aliya Khan, Professor of Clinical Medicine, Divisions of Endocrinology and Metabolism and Geriatrics at McMaster University and Director of the Calcium Disorders Clinic at McMaster University.

Ultragenyx offers a patient assistance program called UltraCare™, to provide ongoing support to patients and their caregivers and to assist them in finding access solutions to Crysvida. The UltraCare team in Canada is available Monday to Friday at 1-833-388-5872 (U-LTRA).

About X-Linked Hypophosphatemia (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 Crysvida

Crysvida is a recombinant fully human monoclonal IgG1 antibody, discovered by Kyowa Hakko Kirin, against the phosphaturic hormone fibroblast growth factor 23 (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 is caused by excessive levels and activity of FGF23. Crysvida is designed to bind to and thereby inhibit the biological activity of FGF23. By blocking excess FGF23 in patients, Crysvida is intended to increase phosphate reabsorption from the kidney and increase the production of vitamin D, which enhances intestinal absorption of phosphate and calcium.

For the pediatric XLH population, Health Canada's approval of Crysvida is supported by 64-week data from Study CL201, a randomized, open-label study in 52 patients ages 5 to 12, which showed that treatment with Crysvida improved rickets, increased serum phosphorus levels, decreased serum alkaline phosphatase activity, and increased growth. The indication is also supported by 40-week data from Study CL205, an open-label study in 13 patients ages 1 to 4. In these patients, Crysvida improved rickets, increased serum phosphorus levels and decreased serum alkaline phosphatase activity.

For the adult XLH indication, Health Canada's approval of Crysvida is supported by 24-week data from Study CL303, a randomized, double-blind, placebo-controlled study in 134 adult XLH patients. Crysvida treatment resulted in a higher proportion of patients achieving serum phosphorus levels above the lower limit of normal, a higher rate of complete healing of active fractures and pseudofractures, and a decline in the WOMAC stiffness score compared to placebo. The adult indication is also supported by data from the 48-week, open-label, single-arm bone biopsy study in 14 adult XLH patients, which showed healing of osteomalacia as demonstrated by decreases in osteoid volume/bone volume, osteoid thickness and mineralization lag time.

Kyowa Hakko Kirin, Kyowa Kirin International, a wholly owned subsidiary of Kyowa Hakko Kirin, and Ultragenyx are collaborating in the development

and commercialization of Crysvita globally, based on the collaboration and license agreement between Kyowa Hakko Kirin and Ultragenyx.

INDICATION AND CLINICAL USE (In Canada)

CRYSVITA (Burosumab Injection) is indicated for the treatment of X-linked hypophosphataemia (XLH) in adult and pediatric patients 1 year of age and older.

Treatment should be initiated and monitored by a health professional experienced in the management of patients with metabolic bone diseases.

Safety and efficacy in geriatric populations have not been established.

CONTRAINDICATIONS

- Do not use CRYSVITA with oral phosphate and active vitamin D analogues.
- Do not initiate CRYSVITA treatment if serum phosphorus is within or above the normal range for age.
- CRYSVITA is contraindicated in patients with severe renal impairment or end stage renal disease because these conditions are associated with abnormal mineral metabolism.

RELEVANT WARNINGS AND PRECAUTIONS

- Hyperphosphataemia and risk of ectopic mineralization
- Injection site reactions
- Vitamin D decrease
- Driving and operating machinery
- Hypersensitivity reactions
- Immunogenicity
- Monitoring and laboratory tests
- Fertility
- Pregnancy and breast-feeding

Please find the Product Monograph at <http://international.kyowa-kirin.com/ca/crysvita/pm/>, which also includes important information relating to adverse reactions and dosing information. The Product Monograph is also available by calling 1-833-388-5872.

About UltragenyxPharmaceutical 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.

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 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.

Forward-Looking Statements

Except for the historical information contained herein, the matters set forth in this press release, including statements related to Ultragenyx's expectations regarding the availability of Crysvita in Canada, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in the clinical drug development process, such as the regulatory approval process, the timing of regulatory filings, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations and the availability or commercial potential of our products and drug candidates. Ultragenyx undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of Ultragenyx in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 6, 2018, and its subsequent periodic reports filed with the Securities and Exchange Commission.

Contact Ultragenyx Pharmaceutical Inc.

Investors & Media
Danielle Keatley
+1-415-475-6876

Contact Kyowa Hakko Kirin Co. Ltd.
Media
Hiroki Nakamura
+81-3-5205-7205
Email: media@kyowa-kirin.co.jp

Contact Kyowa Kirin International PLC
Media
Callum Spreng
Spreng Thomson Ltd. (For Kyowa Kirin International PLC)
+44 (0)141 548 5191
Mobile: +44 (0)7803 970103



Source: Ultragenyx Pharmaceutical Inc.