Ultragenyx and Kyowa Kirin Announce Crysvita® (burosumab-twza) Now Launched in the U.S. for the Treatment of X–linked Hypophosphatemia (XLH) in Children and Adults

April 30, 2018

First FDA-Approved Treatment that Targets the Underlying Cause of this Rare, Hereditary, Lifelong Disease

UltraCare™ Program in Place to Provide Ongoing Patient Support

NOVATO, Calif., TOKYO and LONDON, April 30, 2018 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ:RARE), a biopharmaceutical company focused on the development of novel products for rare and ultra-rare diseases, Kyowa Hakko Kirin Co. Ltd, (Kyowa Hakko Kirin), and Kyowa Kirin International PLC (Kyowa Kirin International) today announced that Crysvita® (burosumab-twza) entered the commercial supply chain in the United States and generated its first sales to specialty pharmacies on April 27, 2018—ten days after its approval by the U.S. Food and Drug Administration (FDA). Crysvita was approved by the FDA for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients one year of age and older. Crysvita is the first drug approved in the United States for XLH—a rare, hereditary, lifelong disease that affects approximately 12,000 people in the U.S.

“With this commercial launch of Crysvita, adults and children living with XLH now have access to the only treatment that targets the underlying cause of this debilitating disorder,” said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. “Our quick transition from approval to product availability demonstrates the urgency we feel about bringing Crysvita to patients. Through the UltraCare™ program, our next job is helping everyone who can benefit from Crysvita to navigate the health-care system and gain access to this new treatment.”

Dr. Tom Stratford, President and CEO of Kyowa Kirin International, said: “We are excited about the benefits Crysvita may bring to people affected by XLH and our U.S. team is looking forward to working alongside our colleagues at Ultragenyx to help make this important product a success.”

The UltraCare™ program offers ongoing support to patients and their caregivers to help them understand insurance coverage and assist them in finding financial support for Crysvita and the administration of Crysvita. Dedicated in-house UltraCare Guides are available Monday through Friday from 9 a.m. to 8 p.m. Eastern Time at 888-756-8657.

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.

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 lower-extremity deformity, delayed growth and decreased height. Adults with XLH have an increased risk of fractures.

About Crysvita

Crysvita 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. Crysvita is designed to bind to and thereby inhibit the biological activity of FGF23. By blocking excess FGF23 in patients, Crysvita 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, the FDA approval of Crysvita 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 Crysvita 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, Crysvita improved rickets and lower-limb deformity, increased serum phosphorus levels and decreased serum alkaline phosphatase activity.

For the adult XLH indication, the FDA approval of Crysvita is supported by 24-week data from Study CL303, a randomized, double-blind, placebo-controlled study in 134 adult XLH patients. Crysvita treatment resulted in a higher proportion of patients achieving serum phosphorus levels above the lower limit of normal, and a higher rate of complete healing of active fractures and pseudofractures, 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.

INDICATION (IN THE U.S.)

Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients one year of age and older.

IMPORTANT SAFETY INFORMATION

Crysvita should not be taken if:

- An oral phosphate supplement and a specific form of vitamin D supplement are taken

- Phosphorus levels from a blood sample are within or above the normal range for age
- Kidney problems are present

What is the most important information to know about Crysvita?

- Some patients developed allergic reactions (rash and hives) while taking Crysvita. Doctors will monitor for symptoms of an allergic reaction while Crysvita is taken.
- High levels of phosphorus in the blood have been reported in some patients taking Crysvita. This may be related to a risk of high calcium levels in the kidneys. Doctors will collect samples to monitor levels.
- Administration of Crysvita may result in reactions at the injection site, such as hives, reddening of the skin, rash, swelling, bruising, pain, severe itching of the skin, and collection of blood outside of a blood vessel (hematoma).

What are the possible side effects of Crysvita?

- The most common adverse reactions that were seen in children with XLH are:
  • Headache
  • Injection site reaction
  • Vomiting
  • Fever
  • Pain in arms and legs
  • Decreased vitamin D levels
  • Rash
  • Toothache
  • Muscle pain
  • Tooth infection
  • Dizziness

- The most common adverse reactions that were seen in adults with XLH are:
  • Back pain
  • Headache
  • Tooth infection
  • Restless leg syndrome
  • Decreased vitamin D levels
  • Dizziness
  • Constipation
  • Phosphorus levels increased in the blood

- Narrowing of the spaces within the spine is common in adults with XLH and pressure on the spinal cord has been reported in adults taking Crysvita. It is not known if taking Crysvita worsens the narrowing of the spaces within the spine or the pressure on the spinal cord.

Before taking Crysvita, doctors should be informed about all medical conditions, including if:

- One is pregnant, thinks she may be pregnant, or plans to become pregnant. There is not enough experience to know if Crysvita may harm an unborn baby. Report pregnancies to the Ultragenyx Adverse Event reporting line at 1-888-756-8657.
- One is breastfeeding or plans to breastfeed. There is not enough experience to know if Crysvita passes into breast milk. Women should talk with their doctors about the best way to feed their babies while taking Crysvita.

While taking Crysvita, doctors should be informed if one experiences:

- An allergic reaction such as rash or hives
- A rash, swelling, bruising or other reaction at the injection site
- New or worsening restless leg syndrome

These are not all the possible side effects of Crysvita. Doctors should be contacted for medical advice about side effects.

Side effects may be reported to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. Side effects may also be reported to Ultragenyx at 1-888-756-8657.

Please see full Prescribing Information for additional Important Safety Information.

About Ultragenyx

Ultragenyx is a biopharmaceutical company committed to bringing to patients novel therapies for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. Founded in 2010, the company has rapidly built a diverse portfolio of approved and investigational

therapies to address diseases for which the unmet medical need is high, the biology for treatment is clear, and 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.

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