Ultragenyx and Kyowa Kirin Announce U.S. FDA Approves Label Update for Crysvita® (burosumab) for the Treatment of X-Linked Hypophosphatemia (XLH)

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Expanded Label Includes Additional Clinical Data Highlighting Superiority Over Conventional Therapy for Pediatric Patients and Extends Current U.S. Indication to Patients Aged Six Months and Older

Expanded Label Includes Data Demonstrating Improvement in Stiffness, Continued Further Healing of Fractures and Maintenance of Efficacy with Longer-Term Treatment in Adults

NOVATO, Calif., and TOKYO, Sept. 30, 2019 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development of novel products for serious rare and ultra-rare diseases, and Kyowa Kirin Co., Ltd. today announced that the U.S. Food and Drug Administration (FDA) has approved a label expansion for Crysvita® (burosumab). The label has been updated to include new clinical data demonstrating superiority of treatment with Crysvita versus oral phosphate and active vitamin D (conventional therapy) in pediatric patients with XLH, and improvement in stiffness, and maintenance of efficacy of Crysvita in adult patients with longer-term treatment. The indication has also been expanded to include infants as young as six months of age.

Crysvita is an antibody that binds to and inhibits the biological activity of fibroblast growth factor 23 (FGF23), restoring renal phosphate reabsorption and increasing the serum concentration of 1,25 dihydroxy vitamin D. It was first approved in the U.S. in April 2018 for the treatment of XLH in adult and pediatric patients one year of age and older.

“We are pleased that the updated Crysvita label includes compelling results from a controlled clinical trial demonstrating that Crysvita is significantly more effective than conventional therapy in normalizing phosphorus levels, reducing rickets and lower leg deformity, and improving growth in children with XLH. Furthermore, longer-term data from a study in adults are included showing important sustained Crysvita efficacy in this life-long disease,” said Camille L. Bedrosian, M.D., Chief Medical Officer of Ultragenyx. “As part of our commitment to support the XLH community, we worked closely with the FDA to update the prescribing information for Crysvita so physicians could make more informed treatment decisions for their patients with XLH and ensure that younger patients could be treated as this disease is present at birth.”

For the pediatric XLH population, the U.S. label update is based on 64-week efficacy and safety data from the randomized active-controlled Phase 3 study of Crysvita compared with oral phosphate and active vitamin D (conventional therapy) in 61 children with XLH. The results showed that Crysvita was superior to conventional therapy for all key efficacy endpoints, showing a meaningful improvement in rickets severity, lower limb deformity and growth. The 64-week safety profile was similar to that observed at 40 weeks and in other Crysvita pediatric XLH studies.

For the adult XLH population, the label update incorporates results from the open-label treatment period of the Phase 3 study in 134 adult patients with XLH through week 48, demonstrating that serum phosphorus levels were maintained with no evidence of loss of effect. The updated label also includes results demonstrating the continued healing of fractures and pseudofractures at week 48 and improvement in the patient-reported outcome of stiffness at week 24. The safety profile is consistent with what has been previously observed in this study, with no new adverse reactions identified during the extended treatment period.

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 (burosumab-twza) is a recombinant fully human monoclonal IgG1 antibody, discovered by Kyowa 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.

Kyowa Kirin and Ultragenyx have been collaborating in the development and commercialization of Crysvita globally based on the collaboration and license agreement between the parties.

INDICATION *(IN THE U.S)*
Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older.

IMPORTANT SAFETY INFORMATION

Crysvita should not be taken if:

- An oral phosphate supplement and/or a specific form of vitamin D supplement are taken (such as calcitriol, paricalcitol, doxercalciferol, calcifediol).
- 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:
  - Fever
  - Injection site reaction
  - Cough
  - Vomiting
  - Pain in arms and legs
  - Headache
  - Tooth infection
  - Dental cavities
  - Diarrhea
  - Decreased vitamin D levels
  - Toothache
  - Constipation
  - Muscle pain
  - Rash
  - Dizziness
  - Nausea
- 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
- Muscle spasms
- 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 medications (including supplements) and medical conditions, including if:

- One is taking oral phosphate and/or active vitamin D (such as calcitriol, paricalcitol, doxercalciferol, calcifediol).
- 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 Kyowa Kirin, Inc. 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 Kyowa Kirin, Inc. at 1-888-756-8657.

Please see full Prescribing Information for additional Important Safety Information.

About Ultragenyx Pharmaceutical, 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 typically no approved therapies treating the underlying disease.

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 Kirin commits to innovate drug discovery driven by state-of-the-art technologies. The company focuses on creating new values in the four therapeutic areas: nephrology, oncology, immunology/allergy and neurology. Under the Kyowa Kirin brand, the employees from 36 group companies across North America, EMEA and Asia/Oceania unite to champion the interests of patients and their caregivers in discovering solutions wherever there are unmet medical needs. You can learn more about the business of Kyowa Kirin at www.kyowakirin.com.

Ultragenyx 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 market opportunities for our products, 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, collaboration with third parties, including our collaboration with Kyowa Kirin, 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 from ongoing regulatory scrutiny related to our commercialized products, potential adverse side effects caused by our products 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 August 2, 2019, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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