



Ultragenyx Announces First Patients Dosed in Phase 3 Program Evaluating Setrusumab (UX143) for the Treatment of Osteogenesis Imperfecta (OI)

July 6, 2023

Pivotal Phase 3 portion of *Orbit* study now enrolling approximately 195 pediatric and young adult patients

Newly initiated Phase 3 *Cosmic* study now enrolling approximately 65 younger pediatric patients

NOVATO, Calif., July 06, 2023 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) today announced that the first patients have been dosed in both of its late-stage clinical trials evaluating setrusumab in pediatric and young adult patients with OI sub-types I, III and IV. The Phase 3 portion of the pivotal Phase 2/3 *Orbit* study is evaluating the effect of setrusumab compared to placebo on annualized clinical fracture rate in patients aged 5 to <26 years. The newly initiated Phase 3 *Cosmic* study is an active-controlled study evaluating setrusumab compared to intravenous bisphosphonate (IV-BP) therapy on annualized total fracture rate in patients aged 2 to <5 years.

"I am extremely encouraged by the recent data from the Phase 2 portion of the *Orbit* study, which includes improvement in biochemical markers and bone density measures that reflect the clinical response we have observed in study participants," stated Thomas Carpenter, M.D., professor of Pediatrics (Endocrinology) and of Orthopaedics and Rehabilitation, Yale School of Medicine. "We are looking forward to evaluating the full clinical potential of setrusumab as this important Phase 3 program moves forward, with hopes for improving therapeutic outcomes in OI."

"Data from the Phase 2 portion of the *Orbit* study demonstrated increases in bone formation and bone mineral density, which are important markers of bone strength, as well as early indications of improved bone health from our investigators," said Eric Crombez, M.D., chief medical officer at Ultragenyx. "Our comprehensive Phase 3 program is designed to study the impact of setrusumab on clinical fracture risk reduction. The two Phase 3 trials will evaluate patients over a broad age range, including the younger pediatric population, where the risk of fracture is higher and where we can potentially have the greatest impact on their future health."

Ultragenyx is leading the clinical development of setrusumab as part of a collaboration and license agreement with Mereo BioPharma Group plc (NASDAQ: MREO), a clinical-stage biopharmaceutical company focused on rare diseases. The companies recently announced positive data from the dose-selection Phase 2 portion of the *Orbit* study showing that setrusumab rapidly induced bone production in OI-affected patients.

U.S. residents can learn more by visiting ultraclinicaltrials.com.

The Setrusumab Phase 3 Program

The global, seamless Phase 2/3 *Orbit* study is evaluating the effect of setrusumab compared to placebo on clinical fracture rate in patients aged 5 to <26 years. In the Phase 2 portion, 24 patients were randomized 1:1 to receive setrusumab at one of two doses to determine the optimal dosing strategy for Phase 3. The pivotal Phase 3 portion of the study will include approximately 195 patients at more than 40 sites across 12 countries, randomized 2:1 to receive setrusumab or placebo, with a primary efficacy endpoint of annualized clinical fracture rate. All patients will transition to an extension period and receive open-label setrusumab after the Phase 3 primary analysis is complete.

The global Phase 3 *Cosmic* study is an open-label, randomized, active-controlled study in patients aged 2 to <5 years evaluating setrusumab compared to intravenous bisphosphonates (IV-BP) therapy on reduction in total fracture rate, including morphometric vertebral fractures. The *Cosmic* study will enroll approximately 65 patients at more than 20 sites across 8 countries.

About Osteogenesis Imperfecta (OI)

Osteogenesis Imperfecta (OI) includes a group of genetic disorders impacting bone metabolism. Approximately 85% to 90% of OI cases are caused by mutations in the *COL1A1* or *COL1A2* genes, leading to either reduced or abnormal collagen and changes in bone metabolism. The collagen mutations in OI can result in increased bone brittleness, which contributes to a high rate of fractures, including at atypical sites. Patients with OI also exhibit increased bone resorption (breakdown of old bone) and inadequate production of new bone, which leads to decreased bone mass, bone fragility and weakness. OI can also lead to bone deformities, abnormal spine curvature, pain, decreased mobility, and short stature. No treatments are approved for OI, which affects approximately 60,000 people in the developed world.

About Setrusumab (UX143)

Setrusumab is a fully human monoclonal antibody that inhibits sclerostin, a protein that acts on a key bone-signaling pathway that inhibits the maturation and activity of bone-forming cells. The goal of blocking inhibitory effects of sclerostin is to increase new bone formation, bone mineral density and bone strength. Sclerostin inhibition also reduces excessive bone resorption, further enhancing its impact on bone density. In mouse models of OI, the use of anti-sclerostin antibodies was shown to stimulate bone formation, improve bone mass and density, and increase bone strength against fracture force testing.

Mereo BioPharma's Phase 2b study (*ASTEROID*) treatment phase of the dose-finding study of setrusumab for the treatment of OI in 112 adults was concluded in 2019. The *ASTEROID* study demonstrated treatment with setrusumab resulted in a clear, dose-dependent and statistically significant effect on bone formation and bone density at multiple anatomical sites among adult participants with OI.

Ultragenyx and Mereo BioPharma are collaborating on the development of setrusumab globally based on the collaboration and license agreement between the parties. The companies have developed a comprehensive late-stage program to continue development of setrusumab in pediatric and young adult patients across OI sub-types I, III and IV.

About Ultragenyx Pharmaceutical Inc.

Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients for the treatment of serious rare and ultrarare 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 [ultragenyx.com](https://www.ultragenyx.com).

Ultragenyx Forward-Looking Statements and Use of Digital Media

Except for the historical information contained herein, the matters set forth in this press release, including statements related to Ultragenyx's expectations and projections regarding its future operating results and financial performance, business plans and objectives for UX143, expectations regarding the tolerability and safety of UX143, and future clinical and regulatory developments for UX143 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, 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 uncertainty of clinical drug development and unpredictability and lengthy process for obtaining regulatory approvals, the ability of the company and Mereo BioPharma to successfully develop UX143, the company's ability to achieve its projected development goals in its expected timeframes, risks related to adverse side effects, risks related to reliance on third party partners to conduct certain activities on the company's behalf, the potential for any license or collaboration agreement, including the company's collaboration agreement with Mereo to be terminated, smaller than anticipated market opportunities for the company's products and product candidates, manufacturing risks, competition from other therapies or products, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations, the company's future operating results and financial performance, the timing of clinical trial activities and reporting results from same, and the availability or commercial potential of Ultragenyx's 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 (SEC) on May 5, 2023, and its subsequent periodic reports filed with the SEC.

In addition to its SEC filings, press releases and public conference calls, Ultragenyx uses its investor relations website and social media outlets to publish important information about the company, including information that may be deemed material to investors, and to comply with its disclosure obligations under Regulation FD. Financial and other information about Ultragenyx is routinely posted and is accessible on Ultragenyx's Investor Relations website (<https://ir.ultragenyx.com/>) and LinkedIn website (<https://www.linkedin.com/company/ultragenyx-pharmaceutical-inc-/>).

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