Ultragenyx and Mereo BioPharma Announce UX143 Phase 3 Orbit Study for Osteogenesis Imperfecta Progressing to Final Analysis

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Data from Orbit and Cosmic studies expected around the end of the year

NOVATO, Calif., July 09, 2025 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) and Mereo BioPharma Group plc (NASDAQ: MREO), today announced that the randomized, placebo-controlled Phase 3 portion of the *Orbit* study evaluating UX143 (setrusumab) in pediatric and young adult patients with osteogenesis imperfecta (OI) is progressing toward a final analysis consistent with the original plan, around the end of the year.

The Data Monitoring Committee (DMC) met and informed the company that UX143 demonstrates an acceptable safety profile and the company should continue the study to the final analysis.

“Based on the feedback we hear from investigators and families who participated in the studies, we are confident that increasing bone mass leads to stronger bone, less fractures, and improved physical abilities,” said Emil D. Kakkis, M.D., Ph.D., chief executive officer and president of Ultragenyx. “While we had hoped to be able to stop the study early, we look forward to having results from both *Orbit* and *Cosmic* around the end of this year.”

Consistent with the statistical analysis plan, data from the *Cosmic* study were not analyzed at this interim timepoint. Study conduct is going well and safety in this younger patient population is consistent with the safety profile in the other studies.

Patients will continue dosing in the ongoing Phase 3 *Orbit* and *Cosmic* clinical studies with the final analyses to be conducted after patients have been on therapy for at least 18-months. The threshold for the Phase 3 *Orbit* final analysis is $p<0.04$ and for the Phase 3 *Cosmic* final analysis is $p<0.05$.

About the Setrusumab Phase 3 Program
Ultragenyx is developing setrusumab in pediatric and young adult patients across OI sub-types I, III and IV with two late-stage studies: the pivotal Phase 2/3 *Orbit* study and Phase 3 *Cosmic* study.

The global, seamless Phase 2/3 *Orbit* study is evaluating the effect of setrusumab on clinical fracture rate in patients aged 5 to 25 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. All patients from the 40 mg/kg dosing cohort have been transitioned to 20 mg/kg of setrusumab.

The pivotal Phase 3 portion of the study has enrolled an additional 159 patients at 45 sites across 11 countries, with subjects randomized 2:1 to receive setrusumab or placebo, and 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 <7 years. Patients are randomized 1:1 to receive setrusumab or intravenous bisphosphonates (IV-BP) therapy to evaluate reduction in the annualized fracture rate. The *Cosmic* study has enrolled 69 patients at 21 sites across 7 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 genetic variants 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. Patients with OI also exhibit inadequate production of new bone and excess bone resorption, resulting in decreased bone mineral density, bone fragility and weakness. OI can also lead to bone deformities, abnormal spine curvature, pain, decreased mobility, and short stature. No treatments are globally approved for OI, which affects approximately 60,000 people in commercially accessible geographies.

About Setrusumab (UX143)
Setrusumab is a fully human monoclonal antibody that inhibits sclerostin, a negative regulator of bone formation. Blocking sclerostin is expected to increase new bone formation, bone mineral density and bone strength in OI. In mouse models of OI, the use of anti-sclerostin antibodies was shown to increase bone formation, improve bone mass to normal levels, and increase bone strength against fracture force testing to normal levels.

In 2019, Mereo BioPharma completed the Phase 2b dose-finding study (ASTEROID) for setrusumab in 112 adults with OI. 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
Ultragenyx is a biopharmaceutical company committed to bringing novel therapies to patients for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved medicines and treatment candidates aimed at addressing diseases with high unmet medical need and clear biology, 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 Mereo BioPharma
Mereo BioPharma is a biopharmaceutical company focused on the development of innovative therapeutics for rare diseases. The Company has two rare disease product candidates: setrusumab for the treatment of osteogenesis imperfecta (OI); and alvelestat for the treatment of severe alpha-1 antitrypsin deficiency-associated lung disease (AATD-LD). The Company's partner, Ultragenyx Pharmaceutical, Inc., has completed enrollment in the Phase 3 portion of a pivotal Phase 2/3 study in pediatrics and young adults (5 to 25 years old) for setrusumab in OI and in the Phase 3 study in pediatric patients (2 to <7 years old). The partnership with Ultragenyx includes potential additional milestone payments of up to $245 million and royalties to Mereo on commercial sales in Ultragenyx territories. Mereo has retained EU and UK commercial rights and will pay Ultragenyx royalties on commercial sales in those territories. Setrusumab has received orphan designation for osteogenesis imperfecta from the European Commission ("EC") and the FDA, PRIME designation from the EMA, and has Breakthrough Therapy designation and rare pediatric disease designation from the FDA. Alvelestat has received Orphan Designation for AATD from the EC and the FDA, and Fast Track designation from the FDA for AATD-LD. Following results from ASTRAEUS and ATALANTa in AATD-lung disease, the Company has aligned with the FDA and the EMA on the primary endpoints for a Phase 3 pivotal study which, if successful, could enable full approval in both the U.S. and Europe. In addition to the rare disease programs, Mereo has two oncology product candidates, etigilimab, an anti-TIGIT; and navicixizumab for the potential treatment of late-line ovarian cancer. Navicixizumab has been partnered with Feng Biosciences, Inc. in a global licensing agreement that includes milestone payments and royalties. Mereo has also entered into an exclusive global license agreement with ReproNovo SA, a reproductive medicine company, for the development and commercialization of leflutrozole, a non-steroidal aromatase inhibitor.

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, including the timing of the final analysis of the Phase 3 studies for UX143 and the outcomes from such studies 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 risk that fast track or breakthrough designations by the FDA may not lead to faster development or regulatory review or approval process and does not increase the likelihood that UX143 will receive marketing approval, 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 7, 2025, 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-/).

Mereo BioPharma Forward-Looking Statements
This press release contains "forward-looking statements" that involve substantial risks and uncertainties. All statements other than statements of historical fact contained herein are forward-looking statements within the meaning of Section 27A of the United States Securities Act of 1933, as amended, and Section 21E of the United States Securities Exchange Act of 1934, as amended. Forward-looking statements usually relate to future events and anticipated revenues, earnings, cash flows or other aspects of our operations or operating results. Forward-looking statements are often identified by the words "believe," "expect," "anticipate," "plan," "intend," "foresee," "should," "would," "could," "may," "estimate," "outlook" and similar expressions, including the negative thereof. The absence of these words, however, does not mean that the statements are not forward-looking. These forward-looking statements are based on the Company's current expectations, beliefs and assumptions concerning future developments and business conditions and their potential effect on the Company. While management believes that these forward-looking statements are reasonable as and when made, there can be no assurance that future developments affecting the Company will be those that it anticipates.

All of the Company's forward-looking statements involve known and unknown risks and uncertainties some of which are significant or beyond its control and assumptions that could cause actual results to differ materially from the Company's historical experience and its present expectations or projections. Such risks and uncertainties include, among others, the uncertainties inherent in the clinical development process; the Company's reliance on third parties to conduct and provide funding for its clinical trials; the Company's dependence on enrollment of patients in its clinical trials; and the Company's dependence on its key executives. You should carefully consider the foregoing factors and the other risks and uncertainties that affect the Company's business, including those described in the "Risk Factors" section of its Annual Report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in the Company's subsequent filings with the Securities and Exchange Commission. The Company wishes to caution you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. The Company undertakes no obligation to publicly update or revise any of our forward-looking statements after the date they are made, whether as a result of new information, future events or otherwise, except to the extent required by law.

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