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# Mereo BioPharma and Ultragenyx Announce Collaboration and License Agreement for Setrusumab in Osteogenesis Imperfecta

*Clinical-stage monoclonal antibody in development for rare genetic bone disease that builds on Ultragenyx's existing bone franchise*

*Ultragenyx leads and funds development to approval; Mereo retains commercial rights in Europe, Ultragenyx commercializes in US and in rest of world*

*Mereo receives $50 million upfront and is eligible for milestones up to $254 million*

**London, Redwood City, Calif., and Novato, Calif. — December 17, 2020 —** Mereo BioPharma Group plc (Nasdaq: MREO, AIM: MPH), a clinical stage biopharmaceutical company focused on oncology and rare diseases, and Ultragenyx Pharmaceutical Inc. (Nasdaq: RARE), a biopharmaceutical company focused on the development and commercialization of novel products for serious rare and ultra-rare diseases, today announced a license and collaboration agreement for setrusumab, a monoclonal antibody in clinical development for osteogenesis imperfecta (OI). Setrusumab is an investigational anti-sclerostin fully human monoclonal antibody that has shown the ability to improve bone production and density leading to greater bone strength in animal models of OI. Data from a Phase 2b of setrusumab conducted by Mereo demonstrated a dose-dependent increase in bone formation, density, and strength in adults with OI.

"Osteogenesis imperfecta is a rare and devastating genetic disease, with currently no approved therapies. We are proud to partner with Ultragenyx to continue the development of setrusumab as potentially the first approved therapy for OI in both children and adults," said Dr. Denise Scots-Knight, Chief Executive Officer of Mereo. "Following the positive data from our Phase 2b ASTEROID study, we set out to find the right partner and we believe that Ultragenyx, with its proven track record of successfully developing and commercializing novel therapies for rare diseases, is ideally positioned to support the further advancement of our innovative therapeutic candidate. We look forward to continuing to work closely with Ultragenyx to make setrusumab available to the OI community worldwide."

"Setrusumab is a great complement to Ultragenyx's product portfolio and enables us to leverage the broad expertise and infrastructure we have established in metabolic bone diseases with Crysvita," stated Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. "Most importantly, setrusumab is a promising option for patients with osteogenesis imperfecta, which is one of the most common genetic bone diseases associated with frequent bone fractures."

OI is a group of genetic disorders including types I, III and IV, of which approximately 85-90% are caused by mutations in the *COL1A1* or *COL1A2* genes leading to either a reduced amount of normal collagen or collagen with abnormal structure and changes in bone metabolism. Since collagen molecules represent the foundation upon which bone is formed, these abnormalities lead to increased bone resorption, reduced bone mass, and bone fragility and weakness. Although the abnormal or deficient collagen weakens bone, these collagen abnormalities also set off a maladaptive cascade of bone remodeling signals that enhance bone resorption, or the breaking down of bone, with inadequate production of new bone, which compounds the bone fragility. These genetic defects and their consequences lead to systemic clinical manifestations such as decreased bone mass, bone brittleness leading to a high rate of fractures, including at atypical sites, or bone deformities, including abnormal spine curvature, as well as pain, decreased mobility, and short stature. OI affects approximately 60,000 patients in the developed world and has no approved treatments.

Setrusumab is a fully human monoclonal antibody that inhibits sclerostin, a protein that acts on a key bone-signaling pathway and inhibits the activity of bone-forming cells. By blocking inhibitory effects of sclerostin, the anti-sclerostin antibody causes new bone formation, increased production of collagen, and increased bone mineral density and strength. Sclerostin inhibition also reduces excessive bone resorption, further enhancing the impact on bone density. In various mouse models of OI, the use of anti-sclerostin antibodies was shown to stimulate bone formation, improve bone mass and density, reduce bone fragility, increase long bone stiffness and strength, and reduce the number of fractures. Overall, improvements in bone mass and strength were enhanced when an anti-sclerostin antibody was used in combination with bisphosphonates, the current standard of care in OI.

Mereo has completed the Phase 2b ASTEROID study of setrusumab across three dose groups monthly for 12 months in 90 adults with OI types I, III, and IV. Results from the study indicated improvements in bone mineral density across multiple measures and at multiple anatomical sites on a dose-dependent basis after 12 months. Improvements were also observed in serum P1NP (procollagen type I N propeptide), a biomarker of bone formation and direct measure of collagen production. The bone mineral density and P1NP results were consistent across OI types studied. In addition, there was a dose-dependent improvement in trabecular bone architecture and bone strength by measuring wrist bone failure load and stiffness. In the per protocol population at the high dose, there was a trend toward improvement of ankle failure load and a statistically significant improvement in ankle bone stiffness. While the study was not powered to show a difference in fracture rates, there was a trend toward a reduction in fractures in the highest dose relative to the lower doses. In the study, setrusumab was generally well tolerated with no cardiac-related safety concerns observed.

The companies will expand and initially prioritize the development of setrusumab for pediatric patients with OI. Development plans are being finalized which may include changes to current study designs, and will require discussions with regulatory agencies, for a pediatric Phase 2/3 study that first focuses on determining the optimal dose based on increases in collagen

production using serum P1NP levels and an acceptable safety profile. Following determination of the dose, the study is intended to adapt into a pivotal Phase 3 stage, evaluating fracture reduction over an estimated 15 to 24 months as the primary endpoint pending regulatory review. The pediatric Phase 2/3 study is expected to start in 2021. A separate pivotal study is also being planned for adults with OI.

Setrusumab has received orphan drug designation from the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA), rare pediatric disease designation from the FDA, and was accepted into the EMA's Priority Medicines program (PRIME).

Under the terms of the collaboration, Ultragenyx will lead future global development of setrusumab in both pediatric and adult patients. Mereo granted Ultragenyx an exclusive license to develop and commercialize setrusumab in the US and rest of the world, excluding Europe where Mereo retains commercial rights. Each party will be responsible for post-marketing commitments in their respective territories.

Ultragenyx will make an upfront payment of $50 million to Mereo and will fund global development of the program until approval, and has agreed to pay a total of up to $254 million upon achievement of certain clinical, regulatory, and commercial milestones. Ultragenyx will pay tiered double digit percentage royalties to Mereo on net sales outside of Europe, and Mereo will pay a fixed double digit percentage royalty to Ultragenyx on net sales in Europe. Under the terms of its 2015 agreement with Novartis, Mereo will pay Novartis a percentage of proceeds, subject to certain deductions, with Mereo receiving a substantial majority of the payments from Ultragenyx.

The completion of the transaction is subject to Hart-Scott-Rodino Antitrust Improvements Act of 1976 (HSR) review and the satisfaction of other customary closing conditions.

**About Osteogenesis Imperfecta**

Osteogenesis Imperfecta (OI) is a rare genetic disorder that is characterized by fragile bones and reduced bone mass resulting in bones that break easily, loose joints, and weakened teeth. In severe cases, those with OI may experience hundreds of fractures in a lifetime. In addition, people with OI often suffer muscle weakness, early hearing loss, fatigue, curved bones, scoliosis, respiratory problems, and short stature, leading to significant effects on overall health and quality of life. The majority of cases of OI (estimated at approximately 90%) are caused by a dominant mutation in a gene coding for type I collagen, a key component of healthy bone. Current treatment of OI is supportive, focusing on minimizing fractures and maximizing mobility, but to date, there are no FDA or EU approved treatments. OI is estimated to affect between 1 in 6,500 and 1 in 30,000 people globally.

**About Mereo Biopharma**

Mereo BioPharma is a biopharmaceutical company focused on the development and commercialization of innovative therapeutics that aim to improve outcomes for oncology and rare diseases. Mereo's lead oncology product candidate, etigilimab (Anti-TIGIT), has completed a Phase 1a dose escalation clinical trial in patients with advanced solid tumors and has been evaluated in a Phase 1b study in combination with nivolumab in select tumor types. The company recently announced initiation of a Phase 1b/2 study of etigilimab in combination with an anti-PD-1/PDL-1 in a range of different tumor types. Mereo's rare disease product portfolio consists of setrusumab, which has completed a Phase 2b dose-ranging study in adults with osteogenesis imperfecta (OI), as well as alvelestat, which is being investigated in a Phase 2 proof-of-concept clinical trial in patients with alpha-1 antitrypsin deficiency (AATD) and in a Phase 1b/2 clinical trial in COVID-19 respiratory disease.

**About Ultragenyx**

Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients 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 and ensuring majority access to its therapies for patients who can benefit.

Ultragenyx's metabolic bone product portfolio includes Crysvita® (burosumab), which is approved by the FDA for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients six months of age and older and for FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older.

For more information on Ultragenyx, please visit the company's website at www.ultragenyx.com.

**Additional Information**

The person responsible for arranging the release of this information on behalf of Mereo BioPharma Group plc is Charles Sermon, General Counsel of Mereo.

**Mereo BioPharma Forward-Looking Statements**

*This Announcement contains "forward-looking statements." All statements other than statements of historical fact contained in this Announcement 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 involve assumptions that could cause actual results to differ materially from the Company's historical experience and its present expectations or projections.*

*These forward-looking statements are subject to risks and uncertainties, including, among other things, those described in the Company's latest Annual Report on Form 20-F, Reports on Form 6-K and other documents filed from time to time by the Company with the United States Securities and Exchange Commission. The Company wishes to caution investors 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 forward-looking statements, whether as a result of new information, future events or otherwise, except to the extent required by law.*

**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 and projections regarding its future operating results and financial performance, anticipated cost or expense reductions, the timing, progress and plans for its clinical programs and clinical studies, future regulatory interactions, and the components and timing of regulatory submissions 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 effects from the COVID-19 pandemic on the company's clinical activities, business and operating*

*results, risks related to reliance on third party partners to conduct certain activities on the company's behalf, uncertainty and potential delays related to clinical drug development, 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 on October 27, 2020, and its subsequent periodic reports filed with the Securities and Exchange Commission.*

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