UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 05, 2023

Ultragenyx Pharmaceutical Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-36276**	**27-2546083**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
60 Leveroni Court Novato, California		**94949**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 415 483-8800

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value	RARE	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On June 5, 2023, Ultragenyx Pharmaceutical Inc. ("Ultragenyx" or the "Company") issued a press release announcing data from the dose-selection Phase 2 portion of the Phase 2/3 Orbit study. The press release is attached hereto as Exhibit 99.1.

The information set forth under Item 7.01 and in the press release attached hereto as Exhibit 99.1 shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01 Other Events.

On June 5, 2023, the Company and Mereo BioPharma Group plc ("Mereo") announced data from the dose-selection Phase 2 portion of the Phase 2/3 Orbit study showing that setrusumab rapidly induced bone production in OI-affected patients. Across all patients evaluated, setrusumab demonstrated statistically significant increases in levels of serum P1NP, a sensitive marker of bone formation, and a substantial and significant improvement in bone mineral density (BMD) by three months.

As of the data cut off, serum P1NP levels through at least 1 month of treatment were available from all 24 patients enrolled in Orbit and demonstrated that treatment with setrusumab significantly increased serum P1NP in both dosing cohorts, peaking at one to two weeks and again, as expected, after the 2-month dosing timepoint. In the 20 mg/kg cohort, there was a mean serum P1NP increase of 57% from baseline over the first month. Because of the higher baseline P1NP level in younger patients, this represents an approximate 8-fold greater increase in serum P1NP over 1 month in pediatric and adolescent patients when compared to adult OI patients. The absolute effect of setrusumab on increasing serum P1NP over the 1-month period with the 20 mg/kg dose, was approximately 80% of the effect achieved with the 40 mg/kg dose, demonstrating a dose response. Patients on placebo at the 1-month timepoint (n=4) showed no significant change in mean serum P1NP from baseline.

The large increase in BMD observed in the Orbit patient population over the first 3 months was consistent with the rapid increase in serum P1NP levels and was similar to results that took 1 year to achieve in the ASTEROID study in adult OI patients. Lumbar spine BMD data were available in 17 of 24 Orbit patients at the 3-month timepoint. Treatment with setrusumab for 3 months resulted in an increase in lumbar spine BMD from baseline of 9.4% at 20 mg/kg (n=10), which represents a substantial mean change in Z-score of +0.65. Treatment with 40 mg/kg (n=7) resulted in a 9.8% BMD increase. Patients on placebo at the 3-month timepoint (n=2) showed no significant change in BMD or change in lumbar spine Z-score.

As of the data cut-off, there have been no treatment-related serious adverse events observed in the study. Reported adverse events have been generally consistent with those observed in the ASTEROID study and include infusion associated events, headache and sinusitis. There have been no reported hypersensitivity reactions related to setrusumab. There were no safety-related differences observed between dosing groups or age groups.

The totality of data demonstrated meaningful response in serum P1NP and BMD across both cohorts, with the majority of the effect observed at 20 mg/kg, which is the dose planned across the setrusumab Phase 3 program. Screening has begun for the Phase 3 portion of the study, which is designed to enroll approximately 195 patients at more than 40 sites across 12 countries.

Cautionary Note Regarding Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of words such as, but not limited to, "anticipates," "continue," "will," or other similar terms or expressions that concern the Company's expectations, plans and intentions. Forward-looking statements include, without limitation, statements regarding the Phase 3 portion of the Orbit study, including expectations regarding enrollment, dosing, endpoints, and other study plans. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's 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, risks related to serious or undesirable side effects of the Company's product candidates, the Company's ability to achieve its projected development goals in its expected timeframes, risks related to reliance on third party partners to conduct certain activities on the Company's behalf, the Company's limited experience in generating revenue from product sales, risks related to product liability lawsuits, 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 the 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 the Company's products and drug candidates. The Company 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 the Company in general, see the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 17, 2023, and its subsequent periodic reports filed with the SEC.

Item 9.01 Financial Statements and Exhibits.

(d) **Exhibits**

Exhibit No.	Description
99.1	Press Release, dated June 5, 2023.
104	The cover page from the Company's Current Report on Form 8-K dated June 5, 2023 formatted in Inline XBRL.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Ultragenyx Pharmaceutical Inc.

Date: June 5, 2023

By: /s/ Emil D. Kakkis, M.D., Ph.D.
Emil D. Kakkis, M.D., Ph.D.

President and Chief Executive Officer

Ultragenyx and Mereo BioPharma Announce Positive Data from the Ongoing Phase 2/3 *Orbit* Study of Setrusumab (UX143) in Osteogenesis Imperfecta (OI)

Pediatric data show substantial induction of bone production in 1 week and a large increase in bone formation within 3 months of initiating monthly setrusumab treatment

Phase 3 sites beginning to screen patients

Conference call to discuss data planned for 5 p.m. Eastern Time

NOVATO, Calif and LONDON, UK — June 5, 2023 — Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) and Mereo BioPharma Group plc (NASDAQ: MREO) today announced data from the dose-selection Phase 2 portion of the Phase 2/3 *Orbit* study showing that setrusumab rapidly induced bone production in OI-affected patients. Across all patients evaluated setrusumab demonstrated statistically significant increases in levels of serum P1NP, a sensitive marker of bone formation, and a substantial and significant improvement in bone mineral density (BMD) by 3 months.

“The rate of increasing bone mineralization we're observing on DXA scans is striking, unlike anything I have typically seen with bisphosphonate therapy. This increase in bone mass underscores the potential to make denser and stronger bone,” said Gary Gottesman, M.D., Professor of Pediatrics and Medicine, Washington University School of Medicine.

As of the data cut off, serum P1NP levels through at least 1 month of treatment were available from all 24 patients enrolled in *Orbit* and demonstrated that treatment with setrusumab significantly increased serum P1NP in both dosing cohorts, peaking at one to two weeks and again, as expected, after the 2-month dosing timepoint. In the 20 mg/kg cohort, there was a mean serum P1NP increase of 57% from baseline over the first month. Because of the higher baseline P1NP level in younger patients, this represents an approximate 8-fold greater increase in serum P1NP over 1 month in pediatric and adolescent patients when compared to adult OI patients. The absolute effect of setrusumab on increasing serum P1NP over the 1-month period with the 20 mg/kg dose, was approximately 80% of the effect achieved with the 40 mg/kg dose, demonstrating a dose response. Patients on placebo at the 1-month timepoint (n=4) showed no significant change in mean serum P1NP from baseline.

The large increase in BMD observed in the *Orbit* patient population over the first 3 months was consistent with the rapid increase in serum P1NP levels and was similar to results that took 1 year to achieve in the ASTEROID study in adult OI patients. Lumbar spine BMD data were available in 17 of 24 *Orbit* patients at the 3-month timepoint. Treatment with setrusumab for 3 months resulted in an increase in lumbar spine BMD from baseline of 9.4% at 20 mg/kg (n=10), which represents a substantial mean change in Z-score of +0.65. Treatment with 40 mg/kg (n=7) resulted in a 9.8% BMD increase. Patients on placebo at the 3-month timepoint (n=2) showed no significant change in BMD or change in lumbar spine Z-score.

“The dramatic lumbar spine BMD improvements in children at 3 months show that growing bones are more dynamic, and we anticipate the potential for a greater effect on bone formation and strength in younger patients with maturing bones,” said Eric Crombez, M.D., chief medical officer at Ultragenyx. “Based on the reports from study investigators, we’re encouraged by the impact setrusumab appears to be having on bone health so far.”

As of the data cut-off, there have been no treatment-related serious adverse events observed in the study. Reported adverse events have been generally consistent with those observed in the ASTEROID study and include infusion associated events, headache and sinusitis. There have been no reported hypersensitivity reactions related to setrusumab. There were no safety-related differences observed between dosing groups or age groups.

The totality of data demonstrated meaningful response in serum P1NP and BMD across both cohorts, with the majority of the effect observed at 20 mg/kg, which is the dose planned across the setrusumab Phase 3 program. Screening has begun for the Phase 3 portion of the study, which is designed to enroll approximately 195 patients at more than 40 sites across 12 countries.

Investor Conference Call and Webcast Information
Ultragenyx will host an investor conference call today, Monday, June 5, at 2 p.m. PT / 5 p.m. ET to discuss the results. The live and replayed webcast of the call will be available through the company’s website at https://ir.ultragenyx.com/events-presentations. To participate in the live call, please register by clicking on the following link (registration link), and you will be provided with dial in details. The replay of the call will be available for one year.

The Setrusumab Phase 3 Program
Ultragenyx and Mereo are developing setrusumab in pediatric and young adult patients across OI sub-types I, III and IV with two late-stage trials: 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 versus placebo on 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 *Orbit* study was designed to be placebo-controlled, however the placebo arm was removed from the Phase 2 portion by amendment. All of the placebo patients enrolled in Phase 2 (n=4) were subsequently rerandomized to one of the dosing cohorts.

The pivotal Phase 3 portion of the study will include approximately 195 patients, 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 Phase 3 *Cosmic* study is an open-label, randomized, active-controlled study in patients aged 2 to <5 years evaluating setrusumab versus intravenous bisphosphonates (IV-BP) therapy on reduction in total fracture rate, including morphometric vertebral fractures. The *Cosmic* study is anticipated to start in the next few months and will enroll approximately 50-66 patients.

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 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) and Bronchiolitis Obliterans Syndrome (BOS). The Company's partner, Ultragenyx Pharmaceutical, Inc., has initiated a pivotal Phase 2/3 pediatric study in young adults (5-25 years old) for setrusumab in OI and expects to initiate a study in pediatric patients (<5 years old) in the next few months. The partnership with Ultragenyx includes potential milestone payments of up to $254 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. Alvelestat has received U.S. Orphan Drug Designation for the treatment of AATD, Fast Track designation from the FDA, and positive data were reported from a Phase 2 proof-of-concept study in North America, Europe and the UK. In addition to the rare disease programs, Mereo has two oncology product candidates in clinical development. Etigilimab (anti-TIGIT) has completed enrollment in a Phase 1b/2 basket study evaluating its safety and efficacy in combination with an anti-PD-1 in a range of tumor types including three rare tumors and three gynecological carcinomas - cervical, ovarian, and endometrial; navicixizumab, for the treatment of late line ovarian cancer, has completed a Phase 1 study and has been partnered with OncXerna Therapeutics, Inc. in a global licensing agreement that includes payments of up to $300 million in milestones and royalties.

For more information on Mereo BioPharma, please visit www.mereobiopharma.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-/mycompany/).

Mereo BioPharma Forward-Looking Statements

This press release contains "forward-looking statements." All statements other than statements of historical fact contained in this press release are forward-looking statements within the meaning of Section 27A of the United States Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the United States Securities Exchange Act of 1934, as amended (the "Exchange Act"). Forward-looking statements usually relate to future events and anticipated revenues, earnings, cash flows or other aspects of Mereo BioPharma's 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 Mereo BioPharma's current expectations, beliefs and assumptions concerning future developments and business conditions and their potential effect on Mereo. While management believes that these forward-looking statements are reasonable as and when made, there can be no assurance that future developments affecting Mereo BioPharma will be those that it anticipates.

All of Mereo BioPharma'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 Mereo BioPharma's historical experience and its present expectations or projections.

Such risks and uncertainties include, among others, the uncertainties inherent in the clinical development process; Mereo BioPharma's reliance on third parties to conduct and provide funding for its clinical trials; Mereo's dependence on enrollment of patients in its clinical trials; and Mereo's dependence on its key executives. You should carefully consider the foregoing factors and the other risks and uncertainties that affect Mereo BioPharma's business, including those described in the "Risk Factors" section of its latest Annual Report on Form 20-F, reports on Form 6-K and other documents furnished or filed from time to time by Mereo BioPharma with the Securities and Exchange Commission. Mereo BioPharma wishes to caution you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. Mereo BioPharma 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.

Contacts

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