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): February 10, 2022

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 2.02 Results of Operations and Financial Condition.

On February 10, 2022, Ultragenyx Pharmaceutical Inc. issued a press release announcing its financial results for the three months ended December 31, 2021 and the year ended December 31, 2021 (the "***Press Release***"). A copy of the Press Release is furnished herewith as Exhibit 99.1

The information set forth under Item 2.02 and in 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 such filing.

Item 9.01 Financial Statements and Exhibits.

(d) **Exhibits**

Exhibit No	**Description**
99.1	Press Release, dated February 10, 2022.
104	The cover page from the Company's Current Report on Form 8-K dated February 10, 2022 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 thereunto duly authorized.

Ultragenyx Pharmaceutical Inc.

Date: Date: February 10, 2022

By: /s/ Mardi C. Dier
Mardi C. Dier
Executive Vice President & Chief Financial Officer

Exhibit 99.1

Contacts Ultragenyx Pharmaceutical Inc.
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Ultragenyx Reports Fourth Quarter and Full Year 2021 Financial Results and Corporate Update

2021 total revenue of $351.4 million and 2021 Crysvita® revenue in Ultragenyx territories[1] of $192.6 million

2022 Crysvita revenue in Ultragenyx territories guidance of $250 million to $260 million and Dojolvi revenue of $55 million to $65 million

Strong Dojolvi® launch continues with approximately 270 patients on reimbursed commercial therapy in the United States as of the end of 2021

Year-end 2021 cash balance of approximately $1.0 billion

NOVATO, Calif. – February 10, 2022 – Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel products for serious rare and ultra-rare genetic diseases, today reported its financial results for the quarter and full year ended December 31, 2021 and reaffirmed its financial guidance for 2022.

“Over the last quarter we made significant progress across our early and late-stage clinical pipeline, including resuming the Phase 1/2 study for Angelman syndrome and initiating two pivotal gene therapy studies in GSDIa and Wilson disease. Our recently announced collaboration with Regeneron for Evkeeza® gives us a fourth approved product adding to the ongoing successful launches of Crysvita, Mepsevii, and Dojolvi,” said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. “In 2022, we will leverage our strong capital position to continue building on this momentum, enrolling patients in our six clinical programs, launching Evkeeza in Europe, expanding our global commercial efforts to Japan, and substantially complete the construction of our gene therapy manufacturing facility.”

Fourth Quarter and Full Year 2021 Financial Results

Net Revenues
For the fourth quarter of 2021, Ultragenyx reported $83.4 million in total revenue. Ultragenyx recognized $55.5 million in Crysvita (burosumab) revenue in the Ultragenyx territories, which includes $50.2 million in collaboration revenue in the North American profit share territory and net product sales in other regions of $5.3 million. Total royalty revenue related to European Crysvita sales were $4.7 million. Dojolvi (triheptanoin) product sales in the fourth quarter of 2021 were $11.8 million. Mepsevii (vestronidase alfa) product sales for the fourth quarter of 2021 were $3.1 million. Total revenue for the fourth quarter also includes $8.2 million of revenue related to the collaboration and license agreement with Daiichi Sankyo that was executed in March 2020.

Revenue for the year ended December 31, 2021 was $351.4 million, including $192.6 million in Crysvita revenue in the Ultragenyx territories. Crysvita collaboration revenue in the North American profit share territory was $171.2 million and net Crysvita product sales in other regions were $21.4 million. Total royalty revenue related to European Crysvita royalties was $18.2 million. Dojolvi product revenue for the year ended December 31, 2021 was $39.6 million. Mepsevii product revenue was $16.0 million. For the year ended December 31, 2021, revenue related to our strategic manufacturing partnership with Daiichi Sankyo was $85.0 million.

Operating Expenses
Total operating expenses for the fourth quarter of 2021 were $186.0 million, including non-cash stock-based compensation of $26.5 million. Total operating expenses for the year ended December 31, 2021 were $733.1 million, which includes a $50.0 million expense for the upfront payment of the license and collaboration agreement with Mereo Biopharma in January 2021 and non-cash stock-based compensation of $105.0 million.

Net Loss
For the fourth quarter of 2021, Ultragenyx reported net loss of $122.5 million, or $1.79 per share basic and diluted, compared with a net loss for the fourth quarter of 2020 of $24.0 million, or $0.37 per share, basic and diluted. For the year ended December 31, 2021, net loss was $454.0 million, or $6.70 per share, basic and diluted, compared with a net loss for the same period in 2020 of $186.6 million, or $3.07 per share, basic and diluted. Net cash used in operations for the year ended December 31, 2021 was $338.7 million.

Cash, Cash Equivalents and Marketable Debt Securities
Cash, cash equivalents, and marketable debt securities were approximately $1.0 billion as of December 31, 2021.

2022 Financial Guidance

The company expects 2022 revenue for Crysvita in Ultragenyx territories to be between $250 million and $260 million and Dojolvi revenue to be between $55 million and $65 million.

Fourth Quarter and Full Year 2021 Revenue and Selected Financial Data Tables

Revenues (dollars in thousands)

	Three Months Ended December 31,		Year Ended December 31,	
	2021	2020	2021	2020
Crysvita Collaboration and Product Revenues:				
North America Collaboration	$ 50,211	$ 37,518	$ 171,198	$ 128,597
ROW Product Sales	5,272	2,914	21,422	10,350
Crysvita in Ultragenyx Territories	55,483	40,432	192,620	138,947
EU Royalty Revenue	4,741	3,567	18,195	14,493
Total Crysvita Revenue	60,224	43,999	210,815	153,440
Dojolvi	11,825	6,390	39,560	13,028
Mepsevii	3,111	3,656	16,035	15,342
Daiichi Sankyo	8,229	37,497	84,996	89,220
Total Revenue	$ 83,389	$ 91,542	$ 351,406	$ 271,030

Selected Financial Data (dollars in thousands, except per share amounts)

	Three Months Ended December 31,		Year Ended December 31,	
	2021	2020	2021	2020
Total revenue	$ 83,389	$ 91,542	$ 351,406	$ 271,030
Operating expense:				
Cost of sales	3,509	5,481	16,008	6,129
Research and development	123,013	131,100	497,153	412,084
Selling, general and administrative	59,431	51,042	219,982	182,933
Total operating expense	185,953	187,623	733,143	601,146
Net loss	$ (122,458)	$ (24,011)	$ (454,025)	$ (186,566)
Net loss per share, basic and diluted	$ (1.79)	$ (0.37)	$ (6.70)	$ (3.07)

Recent Updates and 2022 Milestones

Evkeeza (evinacumab) for Homozygous Familial Hypercholesterolemia (HoFH): Submission of reimbursement dossiers expected in European countries in 2022
Ultragenyx and Regeneron announced a license and collaboration agreement for Ultragenyx to commercialize and distribute Evkeeza in countries outside of the U.S. This includes the European Economic Area where Evkeeza was approved in June 2021 as a

first-in-class monoclonal antibody targeting ANGPTL3 for use together with diet and other low-density lipoprotein-cholesterol (LDL-C) lowering therapies to treat adults and adolescents aged 12 years and older with HoFH.

Ultragenyx plans to submit reimbursement dossiers with national health authorities in Europe in 2022.

UX143 (setrusumab) for Osteogenesis Imperfecta (OI): Dosing in the Pivotal Phase 2/3 Orbit study is expected to begin in the first half of 2022; Phase 2 study in children under age 5 planned for second half of 2022
Ultragenyx expects to begin dosing in the seamless Phase 2/3 Orbit study of UX143 in pediatric and adult patients ages 5 to <26 in the first half of 2022. In addition, Ultragenyx intends to initiate a Phase 2 study in children under age 5 with OI in the second half of 2022 and will continue to evaluate adult patients who were previously treated in the ASTEROID study, a Phase 2b study conducted by our partner Mereo.

A dosing update on the Phase 2 portion of the Orbit study and transition to Phase 3 is expected in the second half of 2022.

DTX401 for Glycogen Storage Disease Type Ia (GSDIa): First patients dosed in Phase 3 GlucoGene study
At the 14th International Congress of Inborn Errors of Metabolism (ICIEM) that took place in November 2021, Ultragenyx presented[2] additional positive long-term safety and efficacy data from its Phase 1/2 study of DTX401 with patients demonstrating a durable response up to three years after receiving DTX401.

The first patients have been dosed in the Phase 3 study of DTX401 following an approximate 4- to 8-week baseline screening period. The Phase 3 GlucoGene study has a 48-week primary efficacy analysis period and the company plans to enroll approximately 50 patients eight years of age and older, randomized 1:1 to DTX401 (1.0 x 10^13 GC/kg dose) or placebo. The primary endpoint is the reduction in oral glucose replacement with cornstarch while maintaining glucose control.

DTX301 for Ornithine Transcarbamylase (OTC) Deficiency: Phase 3 *eNH3ance* study expected to initiate in first half of 2022
At the 14th ICIEM, Ultragenyx presented[3] additional positive long-term safety and efficacy data from its Phase 1/2 study of DTX301 with patients demonstrating a durable response up to four years after receiving DTX301.

Ultragenyx expects to initiate the Phase 3 *eNH3ance* study of DTX301 in patients with OTC in the first half of 2022. The 64-week study will include approximately 50 patients, randomized 1:1 to DTX301 or placebo. The primary endpoints are response as measured by change in baseline disease management and change in 24-hour ammonia levels, supported by change in the rate of ureagenesis as a key secondary endpoint.

GTX-102 for Angelman Syndrome: Phase 1/2 study is titrating patients in Canada and the U.K. with data anticipated mid-year 2022; Dosing has begun in the U.S.
The first four patients in the Phase 1/2 study have received multiple doses of GTX-102 and regular assessments for safety. There have been no treatment-related serious adverse events of any type nor adverse events related to lower extremity weakness observed in these patients, and initial assessments have shown early signs of clinical activity.

The independent data safety monitoring board (DSMB) has met to discuss the assessments for the first two patients each in Cohort 4 (ages 4 to <8 years) and Cohort 5 (ages 8 to <18 years). They recommended that the study continue enrolling and dosing of the remaining planned eight patients has begun. Data on full Cohorts 4 and 5 in the Canada/U.K. arm of the study as well as available safety and efficacy data from the patients treated in the U.S. are anticipated in mid-2022.

Patients naïve to prior treatment with GTX-102 have been screened in the U.S. and dosing has begun.

UX701 for Wilson Disease: Cyprus2+ pivotal Phase 1/2/3 study currently enrolling
Ultragenyx is currently screening and enrolling patients with Wilson disease into the baseline monitoring period prior to dosing in its pivotal, seamless Phase 1/2/3 Cyprus2+ study of UX701. During the first stage of the study, the safety and efficacy of up to three dose levels of UX701 will be evaluated and a dose will be selected for further evaluation in Stage 2. In Stage 2, a new cohort of patients will be randomized 2:1 to receive the selected dose of UX701 or placebo. The primary efficacy endpoints are change in 24-hour urinary copper concentration and percent reduction in standard of care medication by Week 52.

UX053 for Glycogen Storage Disease Type III (GSDIII) Debrancher Deficiency: Phase 1/2 study currently dosing patients; Preliminary data from first part of study and initiation of second part of study anticipated in second half of 2022
Ultragenyx has begun to dose patients in the two-part Phase 1/2 clinical trial evaluating the safety, tolerability and efficacy of UX053 in adults age 18 years and older with GSDIII. Part 1 is open label and will enroll up to 10 patients who will receive a single ascending

dose of UX053 administered via intravenous infusion. Part 2 is double-blind and will evaluate five repeat doses at escalating dose levels in up to 16 patients across four cohorts randomized 3:1 to UX053 or placebo. The primary endpoints are treatment-emergent adverse events (TEAEs), serious TEAEs, and related TEAEs in both parts of the study. Secondary endpoints include pharmacokinetic parameters. Tertiary endpoints include clinician- and patient-reported outcomes, muscle strength, blood sugar, and biomarkers of liver, cardiac and muscle health.

Preliminary data from the Part 1 single ascending dose phase of the study and initiation of the Part 2 repeat dosing phase of the study is anticipated in the second half of the year.

1: Ultragenyx territories include the collaboration revenue from the North American profit share territory (U.S. and Canada) and other regions where revenue from product sales are recognized by Ultragenyx (Latin America, Turkey). This excludes the European territory revenue, which is recognized as non-cash royalty revenue since the rights were sold to Royalty Pharma in December 2019.

2: Derks, T., et. al., (2021, November 22-23). Long-term, sustained efficacy and safety from a phase 1/2 clinical trial of an AAV8-mediated liver-directed gene therapy in adults with glycogen storage disease type Ia. [Conference presentation]. 14th International Congress of Inborn Errors of Metabolism, Sydney, NSW, Australia.

3: Harding, C., et. al., (2021, November 22-23). Safety and efficacy of DTX301, an AAV8 gene therapy, in adults with late-onset ornithine transcarbamylase (OTC) deficiency: results from a phase 1/2 clinical trial. [Conference presentation]. 14th International Congress of Inborn Errors of Metabolism, Sydney, NSW, Australia.

Conference Call and Webcast Information

Ultragenyx will host a conference call today, Thursday, February 10, 2022, at 2 p.m. PT/ 5 p.m. ET to discuss the fourth quarter and year 2021 financial results and provide a corporate update. 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 by phone, dial (855) 797-6910 (USA) or (262) 912-6260 (international) and enter the passcode 2087696. The replay of the call will be available for one year.

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.

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, 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 and commercial activities and 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, the company’s ability to achieve its projected development goals in its expected timeframes, risks and uncertainties related to the regulatory approval process, 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 November 3, 2021, 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/).

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Ultragenyx Pharmaceutical Inc.
Selected Statement of Operations Financial Data
(in thousands, except share and per share amounts)
(unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2021	2020	2021	2020
Statement of Operations Data:				
Revenues:				
Collaboration and license	$ 58,440	$ 75,015	$ 256,438	$ 219,315
Product sales	20,208	12,960	77,017	38,720
Non-cash collaboration royalty revenue	4,741	3,567	17,951	12,995
Total revenues	83,389	91,542	351,406	271,030
Operating expenses:				
Cost of sales	3,509	5,481	16,008	6,129
Research and development	123,013	131,100	497,153	412,084
Selling, general and administrative	59,431	51,042	219,982	182,933
Total operating expenses	185,953	187,623	733,143	601,146
Loss from operations	(102,564)	(96,081)	(381,737)	(330,116)
Change in fair value of equity investments	(16,100)	79,055	(42,063)	170,403
Non-cash interest expense on liability related to the sale of future royalties	(3,804)	(8,198)	(29,422)	(33,291)
Other income, net	30	1,283	241	7,645
Loss before income taxes	$ (122,438)	$ (23,941)	$ (452,981)	$ (185,359)
Provision for income taxes	(20)	(70)	(1,044)	(1,207)
Net loss	$ (122,458)	$ (24,011)	$ (454,025)	$ (186,566)
Net loss per share, basic and diluted	$ (1.79)	$ (0.37)	$ (6.70)	$ (3.07)
Shares used in computing net loss per share, basic and diluted	68,570,546	64,661,831	67,795,540	60,845,550

Ultragenyx Pharmaceutical Inc.
Selected Noncash Activity and License Fees included in Operating Expenses
(in thousands)
(unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2021	2020	2021	2020
Non-cash stock based compensation	$ 26,549	$ 22,813	$ 104,979	$ 85,735
GeneTx purchase option and extension	—	—	—	25,000
REGENXBIO license agreement	—	—	—	8,200
Mereo license and collaboration agreement	—	—	50,000	—

Ultragenyx Pharmaceutical Inc.
Selected Balance Sheet Financial Data
(in thousands)
(unaudited)

	December 31, 2021	December 31, 2020
Balance Sheet Data:		
Cash, cash equivalents, and marketable debt securities	$ 999,129	$ 1,212,039
Working capital	675,236	1,105,695
Total assets	1,522,397	1,759,555
Total stockholders' equity	922,561	1,154,375