

PROSPECTUS SUPPLEMENT

(To Prospectus dated February 12, 2021)

\$350,000,000



Common Stock

We have entered into an Open Market Sale AgreementSM (the "Sale Agreement") with Jefferies LLC ("Jefferies"), relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the Sale Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$350,000,000 from time to time through Jefferies acting as our sales agent.

Our common stock is traded on the Nasdaq Global Select Market under the symbol "RARE." On May 5, 2021, the last reported sale price per share of our common stock was \$106.01.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made through sales deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended (the "Securities Act"). Jefferies is not required to sell any specific amount of our common stock but will act as our sales agent and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal sales and trading practices, on mutually agreed terms between Jefferies and us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Jefferies will receive from us a commission of up to 3.0% of the gross proceeds of any shares of common stock sold under the Sale Agreement. In connection with the sale of our common stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting discounts or commissions. We have agreed to indemnify Jefferies against certain liabilities, including liabilities under the Securities Act, or to contribute payments that Jefferies may be required to make because of such liabilities.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CAREFULLY REVIEW THE RISKS AND UNCERTAINTIES REFERENCED UNDER THE HEADING "RISK FACTORS" BEGINNING ON PAGE S-8 OF THIS PROSPECTUS SUPPLEMENT AND IN THE ACCOMPANYING PROSPECTUS, AND IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS SUPPLEMENT.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

Jefferies

Prospectus Supplement dated May 7, 2021.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 (File No. 333-253008) that we filed with the U.S. Securities and Exchange Commission (the "SEC") on February 12, 2021, using a "shelf" registration process. Under this shelf registration, we may, from time to time, sell common stock and other securities, including in this offering.

This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part consists of the accompanying prospectus, which provides more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus, or any documents incorporated by reference, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus, including the documents incorporated by reference therein. Information in any document we subsequently file that is incorporated by reference shall modify or supersede the information in this prospectus supplement, the accompanying prospectus and documents incorporated by reference prior to such subsequent filing. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents we have referred you to in the section entitled "Where You Can Find More Information" below in this prospectus supplement.

We are responsible for the information contained and incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and Jefferies has not, authorized anyone to give you any other information, and neither we nor Jefferies take any responsibility for any other information that others may give you. We are not, and Jefferies is not, making offers to sell the securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. The information contained and incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering speaks only as of the date of this document, unless the information specifically indicates that another date applies. Neither the delivery of this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering, nor any sale of securities made under these documents, will, under any circumstances, create any implication that there has been no change in our affairs since the date of this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering, nor that the information contained or incorporated by reference is correct as of any time subsequent to the date of such information. You should assume that the information contained and incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of the documents containing the information, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations and prospects may have changed since those dates.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the shares of common stock to which it relates, nor do this prospectus supplement and the accompanying prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

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Unless otherwise indicated, information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus concerning our industry and the markets in which we operate, including market position and market opportunity, is based on information from our management's estimates, as well as from industry publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. However, assumptions and estimates of our future performance, and the future performance of our industry, are subject to numerous known and unknown risks and uncertainties, including those described under the heading "Risk Factors" beginning on page S-8 of this prospectus supplement and in the risk factors incorporated by reference into this prospectus supplement and the accompanying prospectus. These and other important factors could result in our estimates and assumptions being materially different from future results. You should read the information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus completely and with the understanding that future results may be materially different and worse from what we expect. See the information included under the heading "Cautionary Note Regarding Forward-Looking Statements."

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus supplement, the words "Ultragenyx," "we," "us," "our," the "Company" or similar references refer to Ultragenyx Pharmaceutical Inc. and its consolidated subsidiaries; and the term "securities" refers to shares of our common stock.

We own registered trademarks covering the Ultragenyx word mark in the United States and multiple other jurisdictions. In addition, we own a registered trademark in the United States covering a stylized design of our Ultragenyx Pharmaceutical logo. We also own registered trademarks in the United States and other territories relating to our Mepsevii and Dojolvi brand names for vestronidase alfa and triheptanoin, respectively. We additionally have a license from Kyowa Kirin Co., Ltd. to registered trademarks covering the Crysvita brand name for burosumab in the United States, Canada, Turkey, and various Latin American territories.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this prospectus supplement are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words, or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our commercialization, marketing, and manufacturing capabilities and strategy;
- our expectations regarding the timing of clinical study commencements and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the anticipated indications for our product candidates, if approved;
- the potential market opportunities for commercializing our products and product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our products and product candidates, if approved for commercial use;
- the impact of the COVID-19 pandemic and related health measures on our business, financial condition and liquidity;
- estimates of our expenses, revenue, capital requirements, and our needs for additional financing;
- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business, products and product candidates and the integration and performance of any businesses we have acquired or may acquire;
- the initiation, timing, progress, and results of ongoing and future preclinical and clinical studies, and our research and development programs;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and product candidates;
- our ability to maintain and establish collaborations or strategic relationships or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- our financial performance and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- developments and projections relating to our competitors and our industry; and
- other risks and uncertainties, including those listed or incorporated by reference in “Risk Factors.”

Any forward-looking statements in this prospectus supplement reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those discussed below under “Risk Factors” and discussed elsewhere and incorporated by reference in this prospectus supplement. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This prospectus supplement also contains or incorporates by reference estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated

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size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

PROSPECTUS SUPPLEMENT SUMMARY

The items in the following summary are described in more detail later in this prospectus supplement and the accompanying prospectus. This summary provides an overview of selected information and does not contain all of the information you should consider before buying our common stock. Therefore, you should read the entire prospectus supplement and the accompanying prospectus carefully, including the information in our filings with the Securities and Exchange Commission ("SEC") incorporated by reference herein, before deciding to invest in our common stock. Investors should carefully consider the information set forth under "[Risk Factors](#)" beginning on page S-8 of this prospectus supplement and page 3 of the accompanying prospectus and those risks identified in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q. In this prospectus supplement, unless the context otherwise requires, references to "the Company," "we," "us," "our," or "Ultragenyx" refer to Ultragenyx Pharmaceutical Inc. and its consolidated subsidiaries.

Overview

We are a biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of serious rare and ultra-rare genetic diseases. We target diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are typically no approved therapies treating the underlying disease.

The patients we seek to treat have diseases with limited or no treatment options, and we recognize that their lives and well-being are dependent upon our efforts to develop new therapies. For this reason, we are passionate about developing these therapies with the utmost urgency and care.

Corporate History and Information

We were incorporated in California in April 2010 and reincorporated in Delaware in June 2011. Our principal executive offices are located at 60 Leveroni Court, Novato, California 94949. Our telephone number is (415) 483-8800 and our e-mail address is info@ultragenyx.com. Our Internet website address is www.ultragenyx.com. The information on, or that can be accessed through, our web site is not part of this prospectus supplement. We have included our web site address as an inactive textual reference only.

THE OFFERING

Common stock offered by us pursuant to this prospectus supplement	Shares of our common stock having an aggregate offering price of up to \$350,000,000.
Common stock to be outstanding immediately after this offering	Up to 70,741,052 shares of our common stock, assuming sales of 3,301,575 shares of our common stock in this offering at a public offering price of \$106.01 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on May 5, 2021. The actual number of shares of our common stock issued will vary depending on the sales price under this offering.
Plan of distribution	“At the market offering” that may be made from time to time through Jefferies acting as our sales agent. See “Plan of Distribution” for additional information.
Use of proceeds	We intend to use the net proceeds, if any, from this offering to continue to support global commercial launch activities, to advance our clinical programs, to initiate and advance new clinical development programs and to advance our preclinical pipeline toward Investigational New Drug application and beyond. This will include the funding of late-stage, including Phase 3, clinical studies, as well as earlier-stage clinical studies for advancing preclinical programs. We also intend to use a portion of the net proceeds to continue investing in early-stage research capabilities to promote our pipeline growth and to further develop our general infrastructure, including building our own GMP gene therapy manufacturing facility to reduce the costs and increase the speed with which we can execute on our gene therapy programs. Finally, we expect to use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets, including if we exercise our option to acquire GeneTx Biotherapeutics, LLC pursuant to the terms of the unitholder option agreement with them, and to fund the development of such new acquired or in-licensed products and technologies. Any remaining proceeds will be used for other ongoing research and development, working capital and other general corporate purposes. See “Use of Proceeds” for additional information.
Risk factors	You should read and consider the information set forth under the heading “Risk Factors” in this prospectus supplement and in the accompanying prospectus, together with the risk factors and cautionary statements described in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, incorporated by reference herein, before deciding to invest in shares of our common stock.
Nasdaq Global Select Market Symbol	“RARE”

The number of shares of common stock to be outstanding after this offering is based on 67,439,477 shares of common stock outstanding as of March 31, 2021 and excludes:

- 6,623,789 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2021 having a weighted-average exercise price of \$73.19 per share;
- 1,716,017 shares of common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2021;
- 217,556 shares of common stock issuable upon the vesting of performance stock units outstanding as of March 31, 2021;
- 500,000 shares of common stock reserved for issuance under our employment inducement plan as of March 31, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under our employment inducement plan;
- 4,192,549 shares of common stock reserved for issuance pursuant to future equity awards under our 2014 Incentive Plan ("2014 Plan") as of March 31, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2014 Plan; and
- 3,995,536 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan ("2014 ESPP") as of March 31, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2014 ESPP.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding stock options or vesting of restricted stock units or performance stock units as of March 31, 2021.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus supplement or incorporated by reference in this prospectus supplement, including the risks and uncertainties discussed under “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference herein in their entirety. If any of the risks incorporated by reference herein or set forth below occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Relating to this Offering

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If we or our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline. Based upon the number of shares of common stock outstanding as of March 31, 2021, and assuming sales of 3,301,575 shares of our common stock in this offering at a public offering price of \$106.01 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on May 5, 2021, as a result of this offering we would have outstanding a total of approximately 70,741,052 shares of common stock, all of which would be freely tradable (subject to the restrictions in Rule 144 for shares of common stock held by our affiliates). Any shares sold in this offering will be freely tradable, without restriction, in the public market.

We have broad discretion as to the use of proceeds from this offering and may not use the proceeds effectively.

Our management will retain broad discretion as to the allocation of the proceeds and may spend these proceeds in ways in which you may not agree. Because of the number and variability of factors that will determine our use of our existing cash, cash equivalents and short-term investments and the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure of our management to apply these funds effectively could result in unfavorable returns and uncertainty about our prospects, each of which could cause the price of our common stock to decline.

If you purchase shares of our common stock in this offering, you may incur immediate and substantial dilution.

Some or all of the public offering price per share in this offering may exceed the as-adjusted net tangible book value per share of our outstanding common stock. After giving effect to an assumed sale of shares of common stock in the aggregate amount of \$350,000,000 at an assumed public offering price of \$106.01 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on May 5, 2021, and after deducting the commissions and estimated offering expenses payable by us, you would incur immediate and substantial dilution in the amount of \$88.79 per share. In addition, you may also experience additional dilution after this offering on any future equity issuances, including the issuance of common stock under the 2014 Plan. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial additional dilution. See “Dilution” for additional information.

It is not possible to predict the aggregate proceeds resulting from sales made under the Sale Agreement.

Subject to certain limitations in the Sale Agreement and compliance with applicable law, we have the discretion to deliver an issuance notice to Jefferies at any time throughout the term of the Sale Agreement. The number of shares that are sold through Jefferies after delivering an issuance notice, if any, will fluctuate based on a number of factors, including the market price of shares of our common stock during the sales period, the limits we set with Jefferies in any applicable issuance notice and the demand for shares of our common stock during the sales period. Because the price per share of each share of common stock sold pursuant to the Sale Agreement will fluctuate during this offering, it is not currently possible to predict the number of shares of common stock that will be sold or the aggregate proceeds we will raise in connection with those sales under the Sale Agreement, and we may not sell any shares of common stock.

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If securities or industry analysts either do not publish research about us or publish inaccurate or unfavorable research about us, our business or our market, or if they change their recommendations regarding our common stock adversely, the trading price or trading volume of our common stock could decline.

The trading market for our common stock will be influenced in part by the research and reports that securities or industry analysts may publish about us, our business, our market, or our competitors. If one or more of these analysts initiate research with an unfavorable rating or downgrade our common stock, provide a more favorable recommendation about our competitors or publish inaccurate or unfavorable research about our business, our common stock price would likely decline. If any analyst who may cover us were to cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause the trading price or trading volume of our common stock to decline.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$350,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the Sale Agreement with Jefferies as a source of financing.

We intend to use the net proceeds, if any, from this offering to continue to support global commercial launch activities, to advance our clinical programs, to initiate and advance new clinical development programs and to advance our preclinical pipeline toward Investigational New Drug application and beyond. This will include the funding of late-stage, including Phase 3, clinical studies, as well as earlier-stage clinical studies for advancing preclinical programs. We also intend to use a portion of the net proceeds to continue investing in early-stage research capabilities to promote our pipeline growth and to further develop our general infrastructure, including building our own GMP gene therapy manufacturing facility to reduce the costs and increase the speed with which we can execute on our gene therapy programs. Finally, we expect to use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets, including if we exercise our option to acquire GeneTx Biotherapeutics, LLC pursuant to the terms of the unitholder option agreement with them, and to fund the development of such new acquired or in-licensed products and technologies. Any remaining proceeds will be used for other ongoing research and development, working capital and other general corporate purposes. The expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures will depend on numerous factors, including the progress of our clinical trials and other development efforts and other factors described under "Risk Factors" in this prospectus supplement, the accompanying base prospectus and the documents incorporated by reference herein and therein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and management will have broad discretion in the timing and application of the net proceeds.

Pending the use of the net proceeds, we may invest the proceeds in interest-bearing, investment-grade securities, certificates of deposit or government securities.

DILUTION

Dilution represents the difference between the amount per share of common stock paid by purchasers of shares of common stock in this offering and the as-adjusted net tangible book value per share of our common stock immediately after this offering. The data in this section are derived from our balance sheet as of March 31, 2021. Net tangible book value per share of common stock is equal to our total tangible assets less the amount of our total liabilities, divided by the sum of the number of shares of common stock outstanding as of March 31, 2021, excluding shares of common stock underlying outstanding options. Our historical net tangible book value as of March 31, 2021 was approximately \$879.1 million, or \$13.04 per share.

After giving effect to the assumed sale of shares of common stock in the aggregate amount of \$350,000,000 at an assumed public offering price of \$106.01 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on May 5, 2021, and after deducting the commissions and estimated offering expenses payable by us, our as-adjusted net tangible book value as of March 31, 2021 would have been \$1,218.4 million, or \$17.22 per share of common stock. This represents an immediate increase in net tangible book value to existing stockholders of \$4.18 per share of common stock and immediate dilution in net tangible book value to purchasers of shares of common stock in this offering of \$88.79 per share of common stock. The following table illustrates this dilution per share of common stock:

Assumed public offering price per share		\$106.01
Historical net tangible book value per share as of March 31, 2021	\$13.04	
Increase in as-adjusted net tangible book value per share of common stock attributable to new investors	\$ 4.18	
As-adjusted net tangible book value per share after this offering		\$ 17.22
Dilution per share to investors participating in this offering		\$ 88.79

The table above illustrates that an aggregate of 3,301,575 shares of our common stock are sold at a price of \$106.01 per share, the last reported sale price of our common stock on the Nasdaq Global Select Market on May 5, 2021. The shares of common stock sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the assumed price at which the shares of common stock are sold would increase the dilution in net tangible book value per share to purchasers of shares of common stock in this offering to \$89.74 per share, after deducting the commissions and estimated offering expenses payable by us. A decrease of \$1.00 per share in the assumed price at which the shares of common stock are sold would decrease the dilution in net tangible book value per share to purchasers of shares of common stock in this offering to \$87.83 per share, after deducting the commissions and estimated offering expenses payable by us. This information is supplied for illustrative purposes only.

Except as noted above, the foregoing excludes, in each case as of March 31, 2021:

- 6,623,789 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2021 having a weighted-average exercise price of \$73.19 per share;
- 1,716,017 shares of common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2021;
- 217,556 shares of common stock issuable upon the vesting of performance stock units outstanding as of March 31, 2021;
- 500,000 shares of common stock reserved for issuance under our employment inducement plan as of March 31, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under our employment inducement plan;
- 4,192,549 shares of common stock reserved for issuance pursuant to future equity awards under the 2014 Plan as of March 31, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under this plan; and

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- 3,995,536 shares of common stock reserved for future issuance under the 2014 ESPP as of March 31, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2014 ESPP.

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. New investors may experience further dilution if any of our outstanding options are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities in the future.

PLAN OF DISTRIBUTION

We have entered into a Sale Agreement with Jefferies, under which we may offer and sell up to \$350,000,000 of our shares of common stock from time to time through Jefferies acting as agent. Sales of our shares of common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell shares of common stock under the Sale Agreement, we will notify Jefferies of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the Sale Agreement to sell our shares of common stock are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Jefferies is generally anticipated to occur on the second trading day following the date on which the sale was made. Sales of our shares of common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission of up to 3.0% of the aggregate gross proceeds we receive from each sale of our shares of common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Jefferies for the fees of and disbursements to its counsel in an amount not to exceed \$50,000, in addition to certain ongoing disbursements to its counsel. We estimate that the total expenses for the offering, excluding any commissions or fee reimbursement payable to Jefferies under the terms of the Sale Agreement, will be approximately \$205,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on the Nasdaq Global Select Market on the day following each day on which our shares of common stock are sold under the Sale Agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of our shares of common stock on our behalf, Jefferies will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of our shares of common stock pursuant to the Sale Agreement will terminate upon the earlier of (i) the sale of all shares of common stock subject to the Sale Agreement and (ii) the termination of the Sale Agreement as permitted therein. We and Jefferies may each terminate the Sale Agreement at any time upon ten days' prior notice.

This summary of the material provisions of the Sale Agreement does not purport to be a complete statement of its terms and conditions. A copy of the Sale Agreement is filed as an exhibit to a Current Report on Form 8-K filed under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and incorporated by reference in this prospectus supplement.

Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and accordingly, Jefferies may at any time hold long or short positions in such securities.

A prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute the prospectus supplement and the accompanying prospectus electronically.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2020, and the effectiveness of our internal control over financial reporting as of December 31, 2020, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

LEGAL MATTERS

The validity of the common stock being offered in this prospectus supplement will be passed on by Gibson, Dunn & Crutcher LLP, San Francisco, California. Certain legal matters in connection with this offering will be passed upon for the Sales Agent by Latham & Watkins LLP.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Exchange Act, and in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. The SEC maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that site is www.sec.gov. Statements contained in this prospectus supplement as to the contents of any contract or other document are not necessarily complete, and in each instance, we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below:

- Annual Report on [Form 10-K](#) for the year ended December 31, 2020 filed with the SEC on February 12, 2021;
- The information specifically incorporated by reference in our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on February 12, 2021, from our Definitive Proxy Statement on [Schedule 14A](#) relating to our 2021 Annual Meeting of Stockholders, which was filed with the SEC on April 29, 2021;
- Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2021, filed with the SEC on May 5, 2021;
- Current Reports on Form 8-K filed with the SEC on [January 8, 2021](#), [January 21, 2021](#) and [April 16, 2021](#); and
- The description of our common stock contained in our registration statement on [Form 8-A](#) (File No. 001-36276) filed with the SEC on January 24, 2014, including any amendment or report filed for the purpose of updating such description.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act shall be deemed incorporated by reference in this prospectus supplement and to be a part of this prospectus supplement from the date of filing of those documents, with the exception of any portion of any report or document that is not deemed "filed" under such provisions on or after the date of this prospectus supplement, until the earlier of the date on which: (1) all of the securities registered hereunder have been sold; or (2) the registration statement of which this prospectus supplement is a part has been withdrawn.

Under no circumstances will any information filed under current items 2.02 or 7.01 of Form 8-K be deemed incorporated herein by reference unless such Form 8-K expressly provides to the contrary.

Upon written or oral request, we will provide without charge to each person to whom a copy of the prospectus supplement is delivered a copy of the documents incorporated by reference herein (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein). You may request a copy of these filings, at no cost, by writing, calling or emailing us at the contact information set forth below. We have authorized no one to provide you with any information that differs from that contained in this prospectus supplement. Accordingly, we take no responsibility for any other information that others may give you. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date of the front cover of this prospectus supplement.

Ultragenyx Pharmaceutical Inc.
60 Leveroni Court
Novato, California 94949
(415) 483-8800

PROSPECTUS



**Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

Under this prospectus, we or any selling stockholder may offer and sell from time to time, in one or more offerings, an indeterminate number of shares of our common stock, preferred stock, debt securities and warrants or any combination thereof separately or in units. The warrants may be convertible into or exercisable or exchangeable for common stock or preferred stock, the preferred stock may be convertible into or exchangeable for common stock and the debt securities may be convertible into or exchangeable for common stock or preferred stock. Each time securities are offered or sold pursuant to this prospectus, we will describe in a prospectus supplement the securities being offered and sold, as well as the specific terms of the securities.

We or any selling stockholder may offer these securities in amounts, at prices and on terms determined at the time of offering. We or any selling stockholder may sell the securities directly to you, through agents we select, or through underwriters and dealers we select. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement or sales agreement prospectus. Each prospectus supplement will provide the amount, price, terms and plan of distribution relating to the securities to be sold pursuant to such prospectus supplement.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "RARE". The last reported sale price of our common stock on The Nasdaq Global Select Market on February 10, 2021 was \$167.22 per share.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CAREFULLY REVIEW THE RISKS AND UNCERTAINTIES REFERENCED UNDER THE HEADING "[RISK FACTORS](#)" BEGINNING ON PAGE 3 OF THIS PROSPECTUS AS WELL AS THOSE CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND ANY RELATED FREE WRITING PROSPECTUS, AND IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS OR THE APPLICABLE PROSPECTUS SUPPLEMENT.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is February 11, 2021

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We have not authorized anyone to provide you with information other than that contained in or incorporated by reference into this prospectus and any prospectus supplement or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give to you. The information contained in this prospectus is accurate only as of the date of this prospectus, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations, and prospects may have changed since those dates. We are not making offers to sell the securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation.

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission, or the SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration statement, we and/or selling stockholders may offer shares of our common stock and preferred stock, various series of warrants to purchase common stock or preferred stock, debt securities or any combination thereof, from time to time in one or more offerings. This prospectus only provides you with a general description of the securities we and/or selling stockholders may offer. Each time we and/or selling stockholders offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the securities being offered and specific terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. Each such prospectus supplement and any free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents incorporated by reference into this prospectus. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or related free writing prospectus, you should rely on the prospectus supplement or any related free writing prospectus we may authorize to be provided to you. We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the headings “Incorporation of Certain Information by Reference” and “Where You Can Find Additional Information” before you invest in our securities.

Neither we nor any selling stockholder have authorized anyone to provide you with information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We take no responsibility for, and can provide no assurances as to the reliability of, any information not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we or a selling stockholder may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document (unless the information specifically indicates that another date applies) and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading “Where You Can Find Additional Information.”

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus, any applicable prospectus supplement and any related free writing prospectus, the words “Ultragenyx,” “we,” “us,” “our,” the “company” or similar references refer to Ultragenyx Pharmaceutical Inc. and its consolidated subsidiaries; and the term “securities” refers collectively to our common stock, preferred stock, warrants to purchase common stock or preferred stock, debt securities, or any combination of the foregoing securities.

We own registered trademarks covering the Ultragenyx word mark in the United States and multiple other jurisdictions. In addition, we own a registered trademark in the United States covering a stylized design of our Ultragenyx Pharmaceutical logo. We also own registered trademarks in the United States and other territories relating to our Mepsevii and Dojolvi brand names for vestronidase alfa and triheptanoin, respectively. We additionally have a license from KKC to registered trademarks covering the Crysvita brand name for burosumab in the United States, Canada, Turkey, and various Latin American territories.

ABOUT ULTRAGENYX PHARMACEUTICAL INC.

We are a biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of serious rare and ultra-rare genetic diseases. We target diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are typically no approved therapies treating the underlying disease.

The patients we seek to treat have diseases with limited or no treatment options, and we recognize that their lives and well-being are dependent upon our efforts to develop new therapies. For this reason, we are passionate about developing these therapies with the utmost urgency and care.

We were incorporated in California in April 2010 and reincorporated in Delaware in June 2011. Our principal executive offices are located at 60 Leveroni Court, Novato, California 94949. Our telephone number is (415) 483-8800 and our e-mail address is info@ultragenyx.com. Our Internet website address is www.ultragenyx.com. The information on, or that can be accessed through, our web site is not part of this prospectus. We have included our web site address as an inactive textual reference only. Additional information about Ultragenyx can be found on our website and in our periodic and current reports filed with the SEC. Copies of our current and periodic reports filed with the SEC are available online at www.sec.gov and our website at www.ultragenyx.com. For additional information about our company, please refer to other documents we have filed with the SEC and that are incorporated by reference into this prospectus, as listed under the heading "Incorporation of Certain Information by Reference."

RISK FACTORS

Investing in our securities involves a high degree of risk. Before you decide whether to purchase any of our securities, in addition to the other information, documents or reports included in or incorporated by reference into this prospectus and any accompanying prospectus supplement or other offering materials, you should carefully consider the risk factors in the section entitled "Risk Factors" in any prospectus supplement as well as our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference into this prospectus and any prospectus supplement in their entirety, as the same may be amended, supplemented or superseded from time to time by our filings under the Securities Exchange Act of 1934, or the Exchange Act. For more information, see the section entitled "Where You Can Find More Information." These risks could materially and adversely affect our business, results of operations and financial condition and could result in a partial or complete loss of your investment.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and registration statement contain forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this prospectus and registration statement are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words, or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our commercialization, marketing, and manufacturing capabilities and strategy;
- our expectations regarding the timing of clinical study commencements and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the anticipated indications for our product candidates, if approved;
- the potential market opportunities for commercializing our products and product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our products and product candidates, if approved for commercial use;
- the impact of the COVID-19 pandemic and related health measures on our business, financial condition and liquidity;
- estimates of our expenses, revenue, capital requirements, and our needs for additional financing;
- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business, products and product candidates and the integration and performance of any businesses we have acquired or may acquire;
- the initiation, timing, progress, and results of ongoing and future preclinical and clinical studies, and our research and development programs;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and product candidates;
- our ability to maintain and establish collaborations or strategic relationships or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- our financial performance and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- developments and projections relating to our competitors and our industry; and
- other risks and uncertainties, including those listed or incorporated by reference in “Risk Factors.”

Any forward-looking statements in this prospectus and registration statement reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those discussed above under “Risk Factors” and discussed elsewhere and incorporated by reference in this prospectus and registration statement. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This prospectus and registration statement also contain or incorporate by reference estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the

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estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

USE OF PROCEEDS

We intend to use the net proceeds we receive from the sale of securities by us as set forth in the applicable prospectus supplement. Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of securities by any selling stockholder.

DESCRIPTION OF SECURITIES

We and/or any selling stockholder may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any such securities, or any combination thereof from time to time in one or more offerings under this prospectus at prices and on terms to be determined at the time of any offering. This prospectus provides you with a general description of the securities we and/or any selling stockholder may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities.

Common Stock. We may issue shares of our common stock from time to time. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. With certain exceptions, the affirmative vote of a majority of our outstanding shares of capital stock is generally required to take action under our amended and restated certificate of incorporation and amended and restated by-laws.

We are authorized to issue 250,000,000 shares of common stock, par value \$0.001 per share, of which 66,818,520 shares were issued and outstanding as of December 31, 2020.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "RARE". The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our certificate of incorporation, our board of directors is authorized, without action by the stockholders, to designate and issue up to an aggregate of 25,000,000 shares of preferred stock in one or more series. The board of directors can fix the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of delaying or preventing a change in control of our company and might harm the market price of our common stock.

Our board of directors will make any determination to issue such shares based on its judgment as to our best interests and the best interests of our stockholders.

If we issue preferred stock pursuant to this prospectus, we will fix the rights, preferences, privileges, qualifications and restrictions of each series of such preferred stock in the certificate of designations relating to that series. If we issue preferred stock pursuant to this prospectus, we will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designations that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. We urge you to read the prospectus supplement related to any series of preferred stock we may offer, as well as the complete certificate of designations that contains the terms of the applicable series of preferred stock.

Debt Securities. The paragraphs below describe the general terms and provisions of the debt securities we may issue. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus, including any additional covenants or changes to existing covenants relating to such series. The prospectus supplement also will indicate whether the general terms and provisions described in this prospectus apply to a particular series of debt securities. You should read the actual indenture if you do not fully understand a term or the way we use it in this prospectus.

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If we issue debt securities at a discount from their principal amount, then, for purposes of calculating the aggregate initial offering price of the offered securities issued under this prospectus, we will include only the initial offering price of the debt securities and not the principal amount of the debt securities.

We have summarized below the material provisions of the indenture, or indicated which material provisions will be described in the related prospectus supplement. The prospectus supplement relating to any particular securities offered will describe the specific terms of the securities, which may be in addition to or different from the general terms summarized in this prospectus. We have included the form of the indenture as an exhibit to our registration statement of which this prospectus is a part, and it is incorporated into this prospectus by reference. Because the summary in this prospectus and in any prospectus supplement does not contain all of the information that you may find useful, you should read the documents relating to the securities that are described in this prospectus or in any applicable prospectus supplement. Please read "Where You Can Find More Information" in this prospectus to find out how you can obtain a copy of those documents. References below to an "indenture" are references to the indenture, as supplemented, under which a particular series of debt securities is issued. As used under this caption, the term "debt securities" includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indenture.

General

The indenture:

- does not limit the amount of debt securities that we may issue;
- allows us to issue debt securities in one or more series;
- does not require us to issue all of the debt securities of a series at the same time; and
- allows us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series.

The prospectus supplement for each offering of debt securities will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior, senior subordinated or subordinated debt securities;
- the aggregate principal amount of the debt securities being offered and any limit on their aggregate principal amount, and, if the series is to be issued at a discount from its face amount, the method of computing the accretion of such discount;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the full principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into common stock or preferred stock or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate or the method of calculation, how and when the conversion price or exchange ratio may be adjusted, whether conversion or exchange is mandatory, at the option of the holder or at our option, the conversion or exchange period, and any other provision in relation thereto, and any applicable limitations on the ownership or transferability of common stock or preferred stock received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;
- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which we will determine those dates;
- the persons to whom interest will be payable;

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- the basis upon which interest will be calculated if other than that of a 360-day year of twelve 30-day months;
- Any collateral securing the performance of our obligations under the debt securities;
- the place or places where the principal of, premium, if any, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- where notices or demands to or upon us in respect of the debt securities and the applicable indenture may be served;
- any provisions regarding our right to redeem or purchase debt securities or the right of holders to require us to redeem or purchase debt securities;
- any right or obligation we have to redeem, repay or purchase the debt securities pursuant to any sinking fund or analogous provision;
- the currency or currencies (including any composite currency) in which the debt securities are denominated and payable if other than United States dollars, and the currency or currencies (including any composite currency) in which principal, premium, if any, and interest, if any, will be payable, and if such payments may be made in a currency other than that in which the debt securities are denominated, the manner for determining such payments, including the time and manner of determining the exchange rate between the currency in which such securities are denominated and the currency in which such securities or any of them may be paid, and any additions to, modifications of or deletions from the terms of the debt securities to provide for or to facilitate the issuance of debt securities denominated or payable in a currency other than U.S. dollars;
- whether the amount of payments of principal of, premium, if any, or interest on, the debt securities may be determined according to an index, formula or other method and how such amounts will be determined;
- whether the debt securities will be in registered form, bearer form or both, and the terms of these forms;
- whether the debt securities will be issued in whole or in part in the form of a global security and, if applicable, the identity of the depository for such global security;
- any provision for electronic issuance of the debt securities or issuance of the debt securities in uncertificated form;
- whether and upon what terms the debt securities of such series may be defeased or discharged, if different from the provisions set forth in the indenture for the series to which the supplemental indenture or authorizing resolution relates;
- any provisions granting special rights to holders of securities upon the occurrence of such events as specified in the applicable prospectus supplement;
- any deletions from, modifications of, or additions to our events of default or covenants or other provisions set forth in the indenture for the series to which the supplemental indenture or authorizing resolution relates; and
- any other material terms of the debt securities, which may be different from the terms set forth in this prospectus.

We may issue debt securities at a discount below their principal amount and provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as “original issue discount securities.” The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

Neither the Delaware General Corporation Law nor our governing instruments define the term “substantially all” as it relates to the sale of assets. Additionally, Delaware cases interpreting the term “substantially all” rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of “substantially all” of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

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The applicable prospectus supplement will also describe any material covenants to which a series of debt securities will be subject and the applicability of those covenants to any of our subsidiaries to be restricted thereby, which are referred to herein as “restricted subsidiaries.” The applicable prospectus supplement will also describe provisions for restricted subsidiaries to cease to be restricted by those covenants.

Events of Default

Unless the applicable prospectus supplement states otherwise, when we refer to “events of default” as defined in the indentures with respect to any series of debt securities, we mean:

- our failure to pay interest on any debt security of such series when the same becomes due and payable and the continuance of any such failure for a period of 30 days;
- our failure to pay the principal or premium of any debt security of such series when the same becomes due and payable at maturity, upon acceleration, redemption or otherwise;
- our failure or the failure of any restricted subsidiary to comply with any of its agreements or covenants in, or provisions of, the debt securities of such series or the indenture (as they relate thereto) and such failure continues for a period of 60 days after our receipt of notice of the default from the trustee or from the holders of at least 25 percent in aggregate principal amount of the then outstanding debt securities of that series (except in the case of a default with respect to the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of the assets of us (or any other provision specified in the applicable supplemental indenture or authorizing resolution), which will constitute an event of default with notice but without passage of time); or
- certain events of bankruptcy, insolvency or reorganization occur with respect to Ultragenyx or any restricted subsidiary of Ultragenyx that is a significant subsidiary (as defined in the indenture).

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the trustee or the holders of 25% or more in principal amount of the outstanding debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable immediately. However, the holders of at least a majority in principal amount of outstanding debt securities of such series may rescind and annul such declaration and its consequences, except an acceleration due to nonpayment of principal or interest on such series, if the rescission would not conflict with any judgment or decree and if all existing events of default with respect to such series have been cured or waived.

The indenture also provides that the holders of at least a majority in principal amount of the outstanding debt securities of any series, by notice to the trustee, may, on behalf of all holders, waive any existing default and its consequences with respect to such series of debt securities, other than any event of default in payment of principal or interest.

The indenture will require the trustee to give notice to the holders of debt securities within 90 days after the trustee obtains knowledge of a default that has occurred and is continuing. However, the trustee may withhold notice to the holders of any series of debt securities of any default, except a default in payment of principal or interest, if any, with respect to such series of debt securities, if the trustee considers it in the interest of the holders of such series of debt securities to do so.

The holders of a majority of the outstanding principal amount of the debt securities of any series will have the right to direct the time, method and place of conducting any proceedings for any remedy available to the trustee with respect to such series, subject to limitations specified in the indenture.

Amendment, Supplement and Waiver

Without notice to or the consent of any holder, we and the trustee may amend or supplement the indenture or the debt securities of a series:

- to cure any ambiguity, omission, defect or inconsistency;
- to comply with the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of our assets;

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- to provide that specific provisions of the indenture shall not apply to a series of debt securities not previously issued or to make a change to specific provisions of the indenture that only applies to any series of debt securities not previously issued or to additional debt securities of a series not previously issued;
- to create a series and establish its terms;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to release a guarantor in respect of any series which, in accordance with the terms of the indenture applicable to such series, ceases to be liable in respect of its guarantee;
- to add a guarantor subsidiary in respect of any series of debt securities;
- to secure any series of debt securities;
- to add to the covenants of Ultragenyx for the benefit of the holders or surrender any right or power conferred upon Ultragenyx;
- to appoint a successor trustee with respect to the securities;
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act;
- to make any change that does not adversely affect the rights of holders; or
- to conform the provisions of the indenture to the final offering document in respect of any series of debt securities.

The indenture will provide that we and the trustee may amend or supplement any provision of the debt securities of a series or of the indenture relating to such series with the written consent of the holders of at least a majority in principal amount of the outstanding debt securities of such series. However, without the consent of each holder of a debt security the terms of which are directly amended, supplemented or waived, an amendment, supplement or waiver may not:

- reduce the amount of debt securities of such series whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest, including defaulted interest;
- reduce the principal of or extend the fixed maturity of any debt security or alter the provisions with respect to redemptions or mandatory offers to repurchase debt securities of a series in a manner adverse to holders;
- make any change that adversely affects any right of a holder to convert or exchange any debt security into or for shares of our common stock or other securities, cash or other property in accordance with the terms of such security;
- modify the ranking or priority of the debt securities of the relevant series;
- release any guarantor of any series from any of its obligations under its guarantee or the indenture otherwise than in accordance with the terms of the indenture;
- make any change to any provision of the indenture relating to the waiver of existing defaults, the rights of holders to receive payment of principal and interest on the debt securities, or to the provisions regarding amending or supplementing the indenture or the debt securities of a particular series with the written consent of the holders of such series, except to increase the percentage required for modification or waiver or to provide for consent of each affected holder of debt securities of such series;
- waive a continuing default or event of default in the payment of principal of or interest on the debt securities; or
- make any debt security payable at a place or in money other than that stated in the debt security, or impair the right of any holder of a debt security to bring suit as permitted by the indenture.

The holders of a majority in aggregate principal amount of the outstanding debt securities of such series may, on behalf of all holders of debt securities of that series, waive any existing default under, or compliance with, any provision of the debt securities of a particular series or of the indenture relating to a particular series of debt securities, other than any event of default in payment of interest or principal.

Defeasance

The indenture will permit us to terminate all our respective obligations under the indenture as they relate to any particular series of debt securities, other than the obligation to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal of and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

The indenture will also permit us to terminate all of our respective obligations under the indenture as they relate to any particular series of debt securities, including the obligations to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that (A) we have received from, or there has been published by, the Internal Revenue Service a ruling, or (B) since the date such series of debt securities were originally issued, there has been a change in the applicable federal income tax law, in either case to the effect that, and based thereon such opinion of counsel shall state that, holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

In addition, the indenture will permit us to terminate substantially all our respective obligations under the indenture as they relate to a particular series of debt securities by depositing with the trustee money or government obligations sufficient to pay all principal and interest on such series at its maturity or redemption date if the debt securities of such series will become due and payable at maturity within one year or are to be called for redemption within one year of the deposit.

Transfer and Exchange

A holder will be able to transfer or exchange debt securities only in accordance with the indenture. The registrar may require a holder, among other things, to furnish appropriate endorsements and transfer documents, and to pay any taxes and fees required by law or permitted by the indenture.

Concerning the Trustee

The indenture will contain limitations on the rights of the trustee, should it become our creditor, to obtain payment of claims in specified cases or to realize on property received in respect of any such claim as security or otherwise. The indenture will permit the trustee to engage in other transactions; however, if it acquires any conflicting interest, it must eliminate such conflict or resign.

The indenture will provide that in case an event of default occurs and is not cured, the trustee will be required, in the exercise of its power, to use the degree of care of a prudent person in similar circumstances in the conduct of such person's own affairs. The trustee shall be under no obligation to exercise any of the rights or powers vested in it by the indenture at the request or direction of any of the holders pursuant to the indenture, unless such holders shall have offered to the trustee security or indemnity satisfactory to the trustee against the costs, expenses and liabilities which might be incurred by it in compliance with such request or direction.

No Recourse Against Others

The indenture will provide that there is no recourse under any obligation, covenant or agreement in the applicable indenture or with respect to any debt security against any of our or our successor's past, present or future stockholders, employees, officers or directors.

Governing Law

The laws of the State of New York will govern the indenture and the debt securities.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series, from time to time. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from those securities.

If we issue warrants, they will be evidenced by warrant agreements or warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. We urge you to read the prospectus supplement related to any series of warrants we may offer, as well as the complete warrant agreement and warrant certificate that contain the terms of the warrants. If we issue warrants, forms of warrant agreements and warrant certificates relating to warrants for the purchase of common stock, preferred stock and debt securities will be incorporated by reference into the registration statement of which this prospectus is a part from reports we would subsequently file with the SEC.

Units. We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

SELLING STOCKHOLDERS

Selling stockholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire from us, our securities. Such selling stockholders may be parties to registration rights agreements with us, or we otherwise may have agreed or will agree to register their securities for resale. The initial purchasers of our securities, as well as their transferees, pledgees, donees or successors, all of whom we refer to as “selling stockholders,” may from time to time offer and sell our securities pursuant to this prospectus, any applicable prospectus supplement or post-effective amendment.

Information regarding the beneficial ownership of our securities by a selling stockholder, the number of securities being offered by a selling stockholder and the number of securities beneficially owned by a selling stockholder after the applicable offering, where applicable, will be set forth in a prospectus supplement or in a post-effective amendment. The applicable prospectus supplement or post-effective amendment will also disclose whether any of the selling stockholders has held any position or office with, has been employed by or otherwise has had a material relationship with us during the three years prior to the date of the applicable prospectus supplement, or post-effective amendment.

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus from time to time in one or more offerings. Registration of the securities covered by this prospectus does not mean, however, that those securities will necessarily be offered or sold.

We may sell the securities separately or together:

- through one or more underwriters or dealers in a public offering and sale by them;
- directly to investors; or
- through agents.

We may sell the securities from time to time:

- in one or more transactions at a fixed price or prices, which may be changed from time to time;
- at market prices prevailing at the times of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We will describe the method of distribution of any securities issued pursuant to this prospectus, and the terms of any offering pursuant to this prospectus, in the applicable prospectus supplement. Any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

If underwriters are used in the sale of any securities, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions described above. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase the securities will be subject to conditions precedent and the underwriters will be obligated to purchase all of the securities if they purchase any of the securities. We may use underwriters with whom we have a material relationship. We will describe the underwriter(s) in the applicable prospectus supplement, naming the underwriter and the nature of any such relationship.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the applicable prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the applicable prospectus supplement, and the applicable prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of securities an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers, as their agents in connection with the sale of securities. These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. The applicable prospectus supplement will identify any such underwriter, dealer or agent and describe any compensation received by them from us. Any initial public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

Unless otherwise specified in the applicable prospectus supplement, all securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without

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notice. Any common stock sold pursuant to a prospectus supplement will be listed for trading on The Nasdaq Global Select Market or other principal market for our common stock. We may apply to list any series of debt securities, preferred stock or warrants on an exchange, but we are not obligated to do so. Therefore, there may not be liquidity or a trading market for any series of securities.

Any underwriter may engage in over-allotment transactions, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. We make no representation or prediction as to the direction or magnitude of any effect that such transactions may have on the price of the securities. For a description of these activities, see the information under the heading "Underwriting" or "Plan of Distribution" in the applicable prospectus supplement.

Underwriters, broker-dealers or agents who may become involved in the sale of the common stock may engage in transactions with and perform other services for us in the ordinary course of their business for which they receive compensation.

LEGAL MATTERS

The legality of the issuance of the securities being offered hereby and the binding nature of any debt securities or warrants being offered hereby is being passed upon by Gibson, Dunn & Crutcher LLP, San Francisco, California. The legality of the securities will be passed upon by counsel for any underwriters, dealers or agents as may be specified in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2020, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in this registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information contained in other documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents. Any statement contained in any document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus, to the extent that a statement contained in or omitted from this prospectus, or in any other subsequently filed document that also is or is deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. We incorporate by reference the documents listed below which have been filed by us:

1. Our Annual Report on [Form 10-K](#) for the year ended December 31, 2020 (including the portions of our proxy statement for our 2021 annual meeting of stockholders incorporated by reference therein);
2. Our Current Reports on Form 8-K filed with the SEC on [January 8, 2021](#) and [January 21, 2021](#); and
3. The description of our common stock contained in our registration statement on [Form 8-A](#) (File No. 001-36276) filed with the SEC on January 24, 2014, including any amendment or report filed for the purpose of updating such description.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except as to any portion of any report or documents that is not deemed filed under such provisions on or after the date of this prospectus until the earlier of the date on which all of the securities registered hereunder have been sold or the registration statement of which this prospectus is a part has been withdrawn, shall be deemed incorporated by reference in this prospectus and to be a part of this prospectus from the date of filing of those documents.

Nothing in this prospectus shall be deemed to incorporate information furnished but not filed with the SEC pursuant to Item 2.02 or 7.01 of Form 8-K.

Upon written or oral request, we will provide without charge to each person, including any beneficial owner, to whom a copy of the prospectus is delivered a copy of the documents incorporated by reference herein (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein). You may request a copy of these filings, at no cost, by writing or telephoning us at the following address: Ultragenyx Pharmaceutical Inc., 60 Leveroni Court, Novato, California 94949, Attention: Investor Relations, telephone: (415) 483-8800. We have authorized no one to provide you with any information that differs from that contained in this prospectus. Accordingly, you should not rely on any information that is not contained in this prospectus. You should not assume that the information in this prospectus is accurate as of any date other than the date of the front cover of this prospectus.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Exchange Act and in accordance therewith file reports, proxy statements and other information with the SEC. Our filings are available to the public over the Internet at the SEC's website at www.sec.gov, as well as at our website at www.ultragenyx.com. Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete, and in each instance we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference.

* * *

\$350,000,000



Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

May 7, 2021
