Ultragenyx Pharmaceutical Inc.
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The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated February 3, 2015

Prospectus Supplement

(To Prospectus dated February 3, 2015)

$125,000,000

Common Stock

We are offering up to $125,000,000 of shares of our common stock.

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 2, 2015 was $56.74 per share.

We are an emerging growth company, as that term is used in the Jumpstart Our Business Startups Act of 2012, and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and certain filings.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-17.

	Per share	Total
Public offering price	$	$
Underwriting discounts and commissions[(1)]	$	$
Proceeds to Ultragenyx Pharmaceutical Inc., before expenses	$	$

(1) See Underwriters for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

We have granted the underwriters an option for a period of 30 days to purchase up to $18,750,000 of additional shares of our common stock.

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

The underwriters expect to deliver the shares of common stock to purchasers on or about February , 2015.

Morgan Stanley **Cowen and Company** **Jefferies**

Baird **Canaccord Genuity** **JMP Securities**

SunTrust Robinson Humphrey **Wedbush PacGrow Life Sciences**

February , 2015

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Prospectus

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This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering. The second part, the accompanying prospectus, gives more general information, some of which may not apply to this offering. In the event that the description of this offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information contained in this prospectus supplement.

We have not authorized anyone to provide you with information other than that contained in this prospectus, the accompanying prospectus 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. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock. Our business, financial condition, results of operations, and prospects may have changed since that date.

No action is being taken in any jurisdiction outside the United States to permit a public offering of our common stock or possession or distribution of this prospectus in that jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus applicable to that jurisdiction.

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PROSPECTUS SUMMARY

The items in the following summary are described in more detail later in this 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 carefully, including the information in our filings with the Securities and Exchange Commission, or SEC, incorporated by reference in this prospectus, before deciding to invest in our common stock. Investors should carefully consider the information set forth under Risk Factors beginning on page S-17 of this prospectus and those identified in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q. In this prospectus, unless the context otherwise requires, references to the Company, we, us, our, or Ultragenyx refer to Ultragenyx Pharmaceutical Inc.

Overview

We are a clinical-stage biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. We focus on diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies. Since our inception in 2010, we have in-licensed potential treatments for multiple rare genetic disorders. Our strategy, which is predicated upon time- and cost-efficient drug development, allows us to pursue multiple programs in parallel with the goal of delivering safe and effective therapies to patients with the utmost urgency.

Our current pipeline consists of two product categories: biologics, including a monoclonal antibody and enzyme replacement therapies; and small-molecule substrate replacement therapies. Enzymes are proteins that the body uses to process materials needed for normal cellular function, and substrates are the materials upon which enzymes act. When enzymes or substrates are missing, the body is unable to perform its normal cellular functions, often leading to significant clinical disease. Several of our therapies are intended to replace deficient enzymes or substrates and one product candidate is an antibody that decreases the activity of an elevated hormone.

Our biologics pipeline includes the following three product candidates:

KRN23, or UX023, is an antibody targeting fibroblast growth factor 23, or FGF23, intended for the treatment of X-linked hypophosphatemia, or XLH, a rare genetic disease that impairs bone growth. We are developing KRN23 pursuant to our collaboration with Kyowa Hakko Kirin Co., Ltd., or KHK. KHK has completed one Phase 1 study, one Phase 1/2 study, and one longer-term Phase 1/2 study of KRN23 in adults with XLH. We initiated a Phase 2 pediatric study in July 2014. We also expect to continue the clinical development of KRN23 in adults with XLH.

KRN23 is also intended for the treatment of tumor-induced osteomalacia, or TIO. TIO results from typically benign tumors that produce excess levels of FGF23, which can lead to severe hypophosphatemia, osteomalacia, bone fractures, fatigue, bone and muscle pain, and muscle weakness. We intend to initiate a Phase 2 study of KRN23 in six adult inoperable TIO patients in the first half of 2015.

rhGUS, or UX003, is an enzyme replacement therapy we are developing for the treatment of mucopolysaccharidosis 7, or MPS 7, a rare lysosomal storage disease that often leads to multi-system disease, pervasive skeletal disease, and early death. We initiated a Phase 3 clinical study in December 2014.

rhPPCA, or UX004, is an enzyme replacement therapy in preclinical development for galactosialidosis, a rare lysosomal storage disease that can cause multi-system clinical disease similar to MPS 7, including an enlarged liver, joint disease, abnormal bone development, short stature, and early death. We continue preclinical development of rhPPCA.

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Our substrate replacement therapy pipeline includes the following product candidates in development for three diseases:

- Triheptanoin, or UX007, is a synthetic triglyceride with a specifically designed chemical composition being studied as an energy substrate replacement therapy in an international open-label Phase 2 study for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD. LC-FAOD is a set of rare metabolic diseases caused by the inability to convert fat into energy, which leads to low blood sugar, muscle rupture, and heart and liver disease.

- Triheptanoin is also in a Phase 2 study for the treatment of glucose transporter type-1 deficiency syndrome, or Glut1 DS, a rare metabolic disease of brain energy deficiency that is characterized by seizures, developmental delay, and movement disorder.

- SA-ER, or UX001, is an extended-release form of sialic acid in a Phase 2 extension study for the treatment of hereditary inclusion body myopathy, or HIBM, a neuromuscular disorder that causes muscle weakness and wasting. We plan to initiate a Phase 3 clinical study by the second half of 2015 and we intend to file a Marketing Authorization Application, or MAA, seeking conditional approval from the European Medicines Agency, or EMA, for the use of SA-ER in the treatment of HIBM in the second half of 2015.

Our current product candidate pipeline has been either in-licensed from academic institutions or derived from partnerships with other pharmaceutical companies. Our strategy is to acquire and retain global commercialization rights to our products to maximize long-term value, where possible. Over time, we intend to build our own commercial organization, which we believe will be of modest size due to the relatively small number of specialists who treat patients with rare and ultra-rare diseases.

The patients we seek to treat have diseases with limited or no treatment options, and we recognize that their lives and well-being are highly 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 strive to build a company that is faster, better, and smarter about advancing multiple product candidates through approval.

We were founded in April 2010 by our current President and Chief Executive Officer, Emil Kakkis, M.D., Ph.D. We have assembled an experienced team with extensive rare disease drug development and commercialization capabilities. Dr. Kakkis and the team at Ultragenyx have been previously involved at other companies in the development and/or commercialization of many therapies approved or in development for rare metabolic genetic diseases, including Aldurazyme, Naglazyme, Kuvan, and Vimizim (BioMarin); Lumizyme/Myozyme (Sanofi-Genzyme); and asfotase alfa (Enobia; now Alexion).

Our Strategy

Our strategy is to identify, acquire, develop, and commercialize novel products for the treatment of rare and ultra-rare diseases in the United States, the European Union, and select international markets, with the goal of becoming a leading rare disease company. The critical components of our business strategy include the following:

- Focus on rare and ultra-rare diseases with significant unmet medical need;

Focus on diseases and therapies with clear mechanisms of action;

Leverage our experience and relationships to in-license promising product candidates;

Develop and commercialize multiple product candidates in parallel;

Focus on excellent and rapid clinical and regulatory execution; and

Seek to retain global commercialization rights to product candidates.

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Product Candidates

The following table summarizes our product candidate pipeline:

KRN23 (UX023) for the treatment of XLH

KRN23 is a fully human monoclonal antibody administered via subcutaneous injection that is designed to bind and reduce the biological activity of FGF23 to increase abnormally low phosphate levels in patients with X-linked hypophosphatemia, or XLH. Patients with XLH have low serum phosphate levels due to excessive phosphate loss into the urine, which is directly caused by the effect on kidney function of excess FGF23 production in bone cells. Low phosphate levels lead to poor bone mineralization and a variety of clinical manifestations, including rickets leading to bowing and other skeletal deformities, short stature, bone pain and fractures, poor quality bone, and muscle weakness. There is no approved drug therapy or treatment for the underlying cause of XLH. Most patients are managed using frequently divided doses of oral phosphate and vitamin D therapy, which has significant side effects. Oral phosphate/vitamin D replacement therapy requires extremely close monitoring due to the potential for excessive phosphate levels and secondary increases in calcium, which can result in severe damage to the kidneys from excess calcium phosphate deposits and other complications. Additionally, some patients are unable to tolerate the regimen due to the chalky stool that results from taking large amounts of oral phosphate or the high frequency of dosing required.

In August 2013, we entered into a collaboration agreement with KHK to jointly develop and commercialize KRN23 for the treatment of XLH. KHK has conducted one Phase 1 study, one Phase 1/2 study and one longer-term Phase 1/2 study of KRN23 in adults with XLH.

Results from the Phase 1 single dose study in 38 adult XLH patients were presented at the American Society for Bone and Mineral Research, or ASBMR, Annual Meeting in October 2013 and published in the Journal of Clinical Investigation in February 2014. The data demonstrated that KRN23 was well tolerated and increased serum phosphate, or phosphorus. Corresponding changes were observed in renal tubular reabsorption of phosphate. Increases in vitamin D were also observed, suggesting improved intestinal absorption of both phosphate and calcium. Importantly, from a safety perspective, changes were not observed in serum calcium.

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No serious adverse events were reported in the Phase 1 study. There did not appear to be a relationship between the incidence and types of adverse events and the dose administered following a single dose of study drug.

Results from a Phase 1/2 study with up to four escalating doses from 0.05 mg/kg to 0.6 mg/kg in 28 adult XLH patients were presented at the 2014 ICE/ENDO joint meeting of The Endocrine Society and the International Congress on Endocrinology in June 2014. The data demonstrated that repeat doses of KRN23 over four months led to an increase in serum phosphate in 100% of patients, with approximately 89% of patients reaching the low end of the normal range. Peak mean serum phosphorus increased to 3.03 ± 0.42 mg/dL after the fourth dose, which is an approximate 60% increase from the mean of 1.89 ± 0.33 mg/dL at baseline. Comparable increases were observed in mean renal tubular reabsorption of phosphate and mean serum vitamin D levels.

Increases in bone remodeling markers of bone formation and bone resorption were also observed in this Phase 1/2 study. The increase in P1NP (procollagen type I N propeptide) from baseline was statistically significant ($p<0.05$) after all doses and the increase in osteocalcin was statistically significant ($p<0.05$) after the fourth dose. These data support the concept that KRN23 s impact on improving phosphate metabolism will improve bone remodeling, a critical part of creating strong, and properly-formed bones.

Increases in quality of life and disability measures were also observed and we intend to objectively evaluate these in a future randomized controlled study.

Data from the long-term Phase 1/2 study to evaluate KRN23 treatment for an additional 12 doses in 22 adult patients with XLH were presented at the ASBMR Annual Meeting in September 2014. Data from the long-term study demonstrated that the increases in serum phosphate levels, renal tubular reabsorption of phosphate, and serum vitamin D levels observed in the initial four-month Phase 1/2 study were generally sustained during the 12-month extension. All patients continued to demonstrate increases in serum phosphate levels, and 53-86% of subjects in the extension study had serum phosphate levels that reached the normal range after each dose. The mean increases in markers of bone remodeling observed in the prior Phase 1/2 study were also generally sustained.

KRN23 was generally safe and well tolerated over the cumulative treatment period. The most common treatment-related adverse events were injection site reaction, arthralgia, diarrhea, restless legs syndrome, injection site erythema, injection site pain, upper abdominal pain, headache, and decreased neutrophil count (both cases of low neutrophil counts were also observed at baseline and were not associated with any significant infections). Serious adverse events were reported in three subjects but were all considered unrelated to KRN23. One patient discontinued treatment due to nephrolithiasis and one patient discontinued due to restless legs syndrome. There were no clinically significant changes in parathyroid hormone, renal ultrasound or cardiac CT. Serum calcium levels did not change significantly, and mild hypercalcemia was observed intermittently in two subjects. Urinary calcium was not increased, and three subjects had only transient hypercalciuria. No anti-KRN23 antibodies were observed.

In July 2014, we announced the first patient screened and enrolled in the Phase 2 pediatric study of KRN23 in patients with XLH. In November 2014, we reached our target enrollment of 30 prepubertal patients ahead of schedule. The primary objectives of the study are to identify a dose and dosing regimen and to establish the safety profile of treatment with KRN23 in pediatric XLH patients. We will also assess preliminary clinical effects of KRN23 treatment on bone health and deformity as measured by radiographic assessments, growth, muscle strength, and motor function, as well as markers of bone health and patient-reported outcomes of pain, disability, and quality of life.

The study consists of a 16-week individual dose-titration period followed by a 48-week treatment period. The goal of the dose-titration period is to identify the individualized dose of KRN23 required to achieve stable serum phosphorus levels in the target range. Patients will be divided into three cohorts of escalating starting dose levels of KRN23 with

either monthly or biweekly dosing regimens. At the end of the 16-week dose-titration period, patients will receive their individually-optimized dose of KRN23 on a monthly or biweekly basis for the

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48-week treatment period. An interim analysis of safety and pharmacodynamic data will be conducted after 24 weeks of the treatment period, which is equal to 40 weeks after the start of the study. We expect data from the interim analysis to be available in late 2015 or early 2016.

Depending on the results of our Phase 2 pediatric study, we intend to conduct a Phase 3 pediatric study. In our recent meeting with the United States Food and Drug Administration, or FDA, the FDA agreed that blinded radiographic assessments of changes in bone abnormalities, i.e. rickets and bowing, and changes in growth may be used as primary endpoint measures in a potential Phase 3 study in pediatric patients. The FDA also indicated that a Phase 3 study in pediatric patients could be open-label, but recommended inclusion of a standard of care control arm for comparison on a non-inferiority basis. We expect that the final design of a pediatric Phase 3 study would be determined once sufficient safety and efficacy data are available and after further consultation with the FDA.

Given the high turnover and growth of bone during childhood and the critical role phosphate plays in bone growth, pediatric XLH patients have the highest morbidity and potential for benefit in a shorter timeframe. This is consistent with third-party data regarding enzyme replacement therapy in hypophosphatasia, which is another genetic bone disease with poor bone mineralization related to phosphate metabolism caused by a different, unrelated mechanism. We also expect to continue to develop KRN23 in adults with XLH and plan to initiate an adult Phase 2b study in the second half of 2015 that will be conducted in parallel with our Phase 3 pediatric study.

Potential market opportunity

Based on incidence and prevalence rates published in a Danish epidemiologic study and surveys of physicians in the United States, we estimate that there are approximately 3,000 cases of XLH in pediatric patients in the United States. Further, there are an estimated 9,000 cases of XLH in adult patients in the United States. However, we expect that many of these adult patients may not seek treatment if their bone disease is not too severe.

KRN23 (UX023) for the treatment of TIO

KRN23 is also intended for the treatment of tumor-induced osteomalacia, or TIO. TIO results from typically benign tumors that produce excess levels of FGF23, which can lead to severe hypophosphatemia, osteomalacia, bone fractures, fatigue, bone and muscle pain, and muscle weakness. There are cases in which resection of the tumor is not feasible or recurrence of the tumor occurs after resection. In patients for whom the tumor is inoperable, the current standard of care consists of oral phosphate and/or vitamin D replacement. The efficacy of this treatment is often limited, as it does not treat the underlying disease and its benefits must be balanced with monitoring for potential risks such as nephrocalcinosis, hypercalciuria, and hyperparathyroidism. We intend to initiate an open-label, dose-finding Phase 2 clinical study in the first half of 2015. Data from the Phase 2 study is expected in late 2015.

This Phase 2 study will evaluate safety and efficacy in approximately six adult inoperable patients. The primary objectives of the study are to establish the dose, dosing regimen, and safety profile of treatment with KRN23 in TIO patients. Preliminary clinical effects of KRN23 treatment will be evaluated by radiographic assessments, muscle strength, walking ability, and patient-reported measures of pain, disability, and quality of life. Markers of bone health and changes in serum phosphorus and other biochemical measures will also be followed.

The study will consist of a 16-week individual dose-titration period followed by a 32-week treatment period. The goal of the dose-titration period is to identify the individualized dose of KRN23 required to achieve stable serum phosphorus levels in the target range. Patients will receive subcutaneous injections of KRN23 once every four weeks.

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Potential market opportunity

We estimate that there are between 500 and 1,000 patients with TIO in the United States, and that approximately half of all cases are inoperable.

rhGUS (UX003) for the treatment of MPS 7

Recombinant human beta-glucuronidase, or rhGUS, is an intravenous, or IV, enzyme replacement therapy for the treatment of mucopolysaccharidosis 7, or MPS 7, also known as Sly Syndrome. Patients with MPS 7 suffer from severe cellular and organ dysfunction that typically leads to death in the teens or early adulthood. MPS 7 is caused by a deficiency of the lysosomal enzyme beta-glucuronidase, which is required for the breakdown of certain complex carbohydrates known as glycosaminoglycans, or GAGs. The inability to properly break down GAGs leads to their accumulation in many tissues, resulting in a serious multi-system disease. Patients with MPS 7 may have abnormal coarsened facial features, enlargement of the liver and spleen, airway obstruction, lung disease, cardiovascular complications, joint stiffness, short stature, and a skeletal disease known as dysostosis multiplex. In addition, many patients experience progressive lung problems as a result of airway obstruction and mucous production, often leading to sleep apnea and pulmonary insufficiency, and eventually requiring tracheostomy. There are currently no approved drug therapies for MPS 7.

We licensed exclusive worldwide rights to rhGUS-related know-how and cell lines from Saint Louis University in November 2010 and initiated development in 2012. We have conducted preclinical studies to support the chronic IV administration of rhGUS. Administration of rhGUS resulted in substantial distribution of enzyme, as well as reduction in tissue pathology in a wide variety of tissues, including the liver, spleen, lung, heart, kidney, muscle, bone, and brain. No adverse toxicology related to rhGUS was noted in these studies.

In December 2013, we initiated an open-label, Phase 1/2 study in the United Kingdom to evaluate the safety, tolerability, efficacy, and dose of IV administration every other week of rhGUS in up to five patients with MPS 7 who are between five and 30 years of age. The initial 12-week treatment period was followed by a dose-titration period and a long-term extension study.

Interim data from the Phase 1/2 study were presented at the Society for the Study of Inborn Errors of Metabolism, or SSIEM, Annual Symposium in September 2014. Results from the 12-week primary analysis phase showed evidence of clearance of lysosomal storage as indicated by the decline in urinary GAG excretion and the reduction in excess liver size. The decrease in urinary GAG excretion was observed by two weeks after the first dose of rhGUS. Urinary GAG excretion declined by approximately 40-50% from baseline after 12 weeks of treatment at a dose of 2 mg/kg. Decreases in liver size were observed in the two patients who had enlarged livers at baseline. No serious adverse events were observed in the 12-week primary analysis phase and through up to 28 total weeks of treatment. The most common adverse events reported to date are infections and gastrointestinal disorders. No infusion-associated reactions were observed after a total of 38 infusions to date in these three subjects. The data presented at SSIEM were consistent with preliminary data previously presented at the American College of Medical Genetics and Genomics, or ACMG, Annual Clinical Genetics Meeting in March 2014.

We are also supplying rhGUS to investigators who are treating patients under emergency investigational new drug, or eIND, applications. Preliminary results from the treatment of the first patient were presented at the Lysosomal Disease Network s 10 Annual World Symposium in February 2014 and updated results were announced in September 2014. The updated results indicated that a decline in urinary GAG excretion of 50-70% and a sustained reduction in the size of the enlarged liver and spleen were observed through 24 weeks of treatment at a dose of 2 mg/kg. The data also showed improved pulmonary function based on reduced carbon dioxide retention. No serious adverse events or

infusion-associated reactions were observed through 12 infusions.

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The EMA has agreed that approval under exceptional circumstances could be possible for a proposed 12-patient placebo-controlled pivotal study in this disease with urinary GAG levels as a surrogate primary endpoint provided the data was strongly supportive of a favorable benefit/risk ratio. The EMA requested that some evidence or trend in improvement in clinical endpoints be observed to support the primary endpoint, but recognized that a statistically significant result on clinical endpoints was unlikely given the small number of patients expected to be enrolled in the study. Agreement with the FDA was reached that their evaluation of the pivotal Phase 3 study will be based on the totality of the data on a patient-by-patient basis. An investigational new drug, or IND, has been filed with the FDA and we initiated the pivotal Phase 3 study in December 2014.

In addition to the above development plan, we intend to study MPS 7 patients under the age of five years, including potentially younger infants born with hydrops fetalis. Currently, these infants can die within a few months to one year, but enzyme replacement therapy might be able to reduce GAG storage and improve health and survival in these patients.

We initiated a Phase 3 global, randomized, placebo-controlled, blind-start clinical study in December 2014. The Phase 3 study will assess the efficacy and safety of rhGUS in 12 patients between five and 35 years of age. Patients are randomized to one of four groups. One cohort begins rhGUS therapy immediately, while the other three start on placebo and cross over to rhGUS at different predefined time points in a blinded manner. This trial design generates treatment data from all 12 patients. Based on data from the Phase 1/2 study, patients will be dosed with 4 mg/kg of rhGUS every other week for up to a total of 48 weeks, and all groups will receive a minimum of 24 weeks of treatment with rhGUS.

The primary objective of the study is to determine the efficacy of rhGUS as determined by the reduction in urinary GAG excretion after 24 weeks of treatment. The Phase 3 study will also evaluate the safety and tolerability of rhGUS, pulmonary function, walking, stair climb, shoulder flexion, fine and gross motor function, hepatosplenomegaly, cardiac size and function, visual acuity, patient and caregiver assessment of most significant clinical problems, global impressions of change, a multi-domain responder index, and other endpoints.

Data from the Phase 3 study is expected in the first half of 2016. Longer-term 36-week data from the Phase 1/2 study is expected to be presented at the Lysosomal Disease Network s 11th Annual World Symposium in February 2015. Two additional patients continue to be treated under eIND applications.

Potential market opportunity

Through our ongoing survey work with metabolic clinics, we have identified approximately 100 potential MPS 7 patients worldwide to date. Based on our experiences with other MPS diseases, we expect that, over time, more patients will be identified during patient identification efforts globally, potentially resulting in up to approximately 200 patients in the developed world.

rhPPCA (UX004) for the treatment of galactosialidosis

Recombinant human protective protein cathepsin-A, or rhPPCA, which was in-licensed from St. Jude Children s Research Hospital in September 2012, is in preclinical development as an enzyme replacement therapy for galactosialidosis, a rare lysosomal storage disease for which there are currently no approved drug therapies. Similar to MPS patients, patients with galactosialidosis present with both soft tissue storage in the liver, spleen, and other tissues, as well as connective tissue (bone and cartilage) related disease. As with MPS 7, an enzyme deficiency results in accumulation of substrates in the lysosomes, causing skeletal and organ dysfunction, and death. We are continuing preclinical development of rhPPCA.

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Triheptanoin (UX007) for the treatment of LC-FAOD

We are developing triheptanoin for oral administration intended as a substrate replacement therapy for patients with long-chain fatty acid oxidation disorders, or LC-FAOD. Triheptanoin is a medium odd-chain triglyceride of seven-carbon fatty acids designed to provide substrate replacement for fatty acid metabolism and restore production of energy. Patients with LC-FAOD have a deficiency that impairs the ability to produce energy from fat, which can lead to depletion of glucose in the body, and severe liver, muscle, and heart disease, as well as death. There are currently no approved drugs or treatments specifically for LC-FAOD. The current standard of care for LC-FAOD includes diligent prevention of fasting combined with the use of low-fat/high-carbohydrate diets, carnitine supplementation in some cases, and medium even-chain triglyceride oil supplementation. Despite treatment with the current standard of care, many patients continue to suffer significant morbidity and mortality.

We licensed certain intellectual property rights for triheptanoin from Baylor Research Institute in August 2012. Triheptanoin has been studied clinically for 13 years in approximately 130 human subjects affected by a variety of diseases, including more than 60 patients with LC-FAOD. Multiple investigator-sponsored open-label studies suggest clinical improvements with triheptanoin treatment, even for patients who were on standard of care. We recently presented a retrospective medical record review study assessing the clinical outcome of triheptanoin treatment on LC-FAOD subjects who have been participating in a compassionate use program at the University of Pittsburgh Medical Center. The data showed that treatment with triheptanoin appeared to reduce the frequency and severity of hospitalizations previously experienced by these patients for disease-related causes, including muscle rupture, hypoglycemia, and cardiomyopathy. Among a number of results suggesting significant improvement after crossing over onto triheptanoin treatment, a reduction in mean total hospital days per year from 17.55 to 5.40 (69%; $p = 0.0242$) was observed after transitioning from standard of care to triheptanoin therapy. These results are clinically important but are derived from a retrospective medical review, and not from a randomized controlled study. The preliminary results of our retrospective medical review are as follows:

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Triheptanoin is currently being evaluated in a prospective international open-label Phase 2 study in up to 30 severely affected LC-FAOD patients. The principal goals of the study are to determine the appropriate clinical endpoints and patient population for testing in potential later-stage pivotal studies. The study will evaluate patients, ages 6 months to 35 years, exhibiting significant clinical manifestations of LC-FAOD despite current therapy. Prior to initiating treatment with triheptanoin, subjects will continue current therapy for four weeks to establish their baseline condition. Triheptanoin will then be titrated to an expected target dose of 25-35% of total daily caloric intake via oral administration, while ensuring tolerability. The study will assess the impact of triheptanoin on several endpoints, including cycle ergometer performance, 12-minute walk test, muscle strength, creatine kinase levels, hypoglycemia, liver size, cardiac disease, and major medical events. The patients will be followed to evaluate the effects of triheptanoin treatment on acute clinical pathophysiology associated with LC-FAOD over 24 weeks, then may continue treatment for an additional 54 weeks for observation of major medical events. We expect interim data from this study to be available in the second half of 2015.

Potential market opportunity

Based upon data from the National Newborn Screening Information System, we estimate that there are approximately 2,000 to 3,500 LC-FAOD patients in the United States, depending on the assumed mortality rate. It is unclear how many of these patients are currently diagnosed because the availability of newborn screening in all 50 states in the United States is a relatively new development. Furthermore, until additional clinical development of triheptanoin is conducted, it is not clear which subsets of diagnosed patients would be considered by clinicians to be good candidates for triheptanoin treatment. Outside of the United States, where newborn screening is not consistently done, estimates of the prevalence of LC-FAOD are more uncertain.

Triheptanoin (UX007) for the treatment of Glut1 DS

We are also developing triheptanoin for patients with glucose transporter type 1 deficiency syndrome, or Glut1 DS. Glut1 DS is caused by a mutation affecting the gene for Glut1, a protein that transports glucose from the blood into the brain. Because glucose is the primary source of energy for the brain, Glut1 DS results in a chronic state of brain energy deficiency and is characterized by seizures, developmental delay, and movement disorder. There are currently no approved drugs specific to Glut1 DS. The current standard of care for Glut1 DS is the ketogenic diet, an extreme high-fat (70-80% of daily calories as fat)/low-carbohydrate diet, which generates ketone bodies as an alternative energy source to glucose, and one or more antiepileptic drugs. The ketogenic diet can be effective in reducing seizures but compliance can be difficult, and the diet has demonstrated limited effectiveness in the treatment of developmental delay and movement disorders. In addition, ketogenic diet can lead to side effects including renal stones. In general, Glut1 DS patients are considered relatively refractory to antiepileptic drugs with only approximately 8% achieving seizure control on antiepileptic drugs alone. There are currently no antiepileptic drugs approved specifically for patients with Glut1 DS.

Triheptanoin is intended as a substrate replacement therapy to provide an alternative source of energy to the brain in Glut1 DS patients. There are open-label investigator-sponsored clinical studies ongoing and there is one publication presenting data on absence seizure reduction and improved developmental function in some Glut1 DS subjects taking triheptanoin.

In March 2014, we initiated a Phase 2 global, randomized, double-blind, placebo-controlled, parallel-group study that may enroll up to 40 patients who are currently not fully compliant with ketogenic diet and continue to have seizures. The primary efficacy objective is the reduction in frequency of seizures compared to placebo following a six-week baseline period and subsequent eight-week placebo-controlled treatment period. Other efficacy objectives include cognitive function and movement disorder. The blinded treatment period will be followed by an open-label extension

period in which patients will be treated with triheptanoin through week 52. Based on recently published results and in order to accelerate enrollment, we are planning to amend the

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enrollment criteria to also include patients with only absence seizures. We expect to release interim data from this study in the second half of 2015. We are exploring additional studies in patients with additional disease manifestations and diet regimens based on investigator feedback.

We also continue to support investigator-sponsored studies that are evaluating triheptanoin across multiple indications.

Potential market opportunity

While a comprehensive genetic analysis of birth incidence has not been conducted, published literature suggests a range of 3,000 to 7,000 Glut1 DS patients in the United States based on evaluations of generalized or absence seizures. The increasing recognition of alternative or variable motor forms of the disease suggests that older patients may be discovered over time. Given that the disease can be inherited as an autosomal dominant disease, the discovery of one patient may be used to identify other affected relatives in some cases, which can be important in marketing of the product.

SA-ER (UX001) for the treatment of HIBM

We are developing an extended-release, oral formulation of sialic acid, or SA-ER, for the treatment of hereditary inclusion body myopathy, or HIBM, which is also known as GNE myopathy. HIBM is characterized by severe progressive muscular myopathy, or disease in which muscle fibers do not function properly, with onset typically in the late teens or twenties. Patients with HIBM have a genetic defect in the gene coding for a particular enzyme that is involved in the first step in the biosynthesis of sialic acid. Therefore, HIBM patients have a sialic acid deficiency, which interferes with muscle function, leading to myopathy and atrophy. Patients typically lose a substantial amount of muscle function within ten to 20 years of diagnosis. There is no approved drug therapy for HIBM.

We are studying SA-ER as a potential substrate replacement therapy designed to address sialic acid deficiency and restore muscle function in HIBM patients. We have conducted a Phase 2 randomized, double-blind, placebo-controlled study of SA-ER in 47 HIBM patients. Data from this study were presented at the American Academy of Neurology Annual Meeting in April 2014. Patients in the study were initially randomized to receive placebo, three grams, or six grams of SA-ER per day. After 24 weeks, placebo patients crossed over to either three grams or six grams total daily dose, on a blinded basis, for an additional 24 weeks. The final analysis compared change at week 48 from baseline for the combined groups at six grams versus three grams of SA-ER. Assessments included pharmacokinetics, composites of upper extremity and lower extremity muscle strength as measured by dynamometry, other clinical endpoints, patient reported outcomes, and safety.

At 24 weeks, assessments of upper extremity composite of muscle strength showed a statistically significant difference in the six gram group compared to placebo (+2.33 kg; 5.5% relative difference from baseline; p=0.040). At 48 weeks, a statistically significant difference between the combined six gram group and the combined three gram group was observed (+3.44 kg; 8.5% relative difference from baseline; p=0.0033). Patients with less advanced disease (able to walk more than 200 meters at baseline), a predefined subset, showed a more pronounced difference (+4.69 kg; 9.6% relative difference from baseline; p=0.00055). The lower extremity composite showed a similar pattern of response but did not show a statistically significant difference between the dose groups. None of the groups showed a significant decline in the lower extremity composite during the treatment period. A positive trend was seen in patient-reported outcomes of functional activity consistent with the potential clinical meaningfulness of the muscle strength assessment. SA-ER appeared to be well tolerated with no serious adverse events observed to date in either dose group, and no dose-dependent treatment-emergent adverse events were identified. Most adverse events were mild to moderate and most commonly were gastrointestinal in nature and pain related to muscle biopsy procedures.

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We continued to treat these patients in an extension study evaluating an increased daily dosage of sialic acid based on the dose dependence observed at weeks 24 and 48. Interim data from the extension study were presented at the International Congress of the World Muscle Society, or WMS, in October 2014. In the first part of the extension study, all 46 patients who completed the 48-week Phase 2 study crossed over to 6 grams for a variable period of time that was on average 24 weeks. In the second part of the extension study, all 46 patients and 13 treatment-naïve patients received 12 grams of SA-ER for 24 weeks. The results presented at WMS include the 49 out of 59 patients who had 24 weeks of data at the higher dose. While the 12 grams data do not suggest any clinically meaningful advantage over 6 grams, the 12 gram data do provide additional data that support clinical activity with SA-ER treatment. The higher dose appeared to be generally safe and well tolerated with no drug-related serious adverse events, but the rate of mild to moderate gastrointestinal adverse events did appear to be greater with this dose. Over the entire approximate two-year study, treatment with SA-ER appeared to slow the progression of upper extremity disease when compared to the 24-week placebo group extrapolated out to two years.

We recently completed an End-of-Phase 2 meeting with the FDA regarding a potential randomized placebo-controlled 48-week single pivotal study of SA-ER in HIBM patients. The FDA agreed with the proposed Phase 3 study design, including the primary endpoint of a composite of upper extremity muscle strength, with supportive secondary endpoint data from a patient-reported outcome, both of which were studied in the Phase 2 study. We plan to initiate the Phase 3 trial, which we anticipate will include approximately 80 patients, during the second half of 2015.

We also intend to file an MAA seeking conditional approval from the EMA for the use of six grams per day of SA-ER tablets in the treatment of HIBM. Based on Scientific Advice recently received from the EMA s Committee for Medicinal Products for Human Use, we intend to file an MAA in the second half of 2015 for stabilization of upper extremity muscle strength.

Potential market opportunity

Approximately 400 HIBM cases have been reported in the published literature. HIBM is expected to occur in one in every 1,600 persons of Persian Jewish descent. Patients have also been identified in Asian Indian, European, Chinese, Japanese, Korean, and Middle Eastern populations. To better understand the patient population, we conducted an initial survey of 420 myopathy clinics in the United States, and the extrapolated results suggest a patient population of approximately 2,000 worldwide.

Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section entitled Risk Factors immediately following this prospectus summary and in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, incorporated by reference herein. These risks include, among others:

- We are a development-stage company and have a limited operating history on which to assess our business, have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future;

- We are heavily dependent upon the success of our product candidates, which are in the early stages of clinical development, and we cannot provide any assurance that any of our product candidates will receive

regulatory approval;

Because the target patient populations of our product candidates are small, and the addressable patient populations potentially even smaller, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth;

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Even if this offering is successful, we expect that we will need to raise additional funding before we can expect to become profitable from sales of our products;

The insurance coverage and reimbursement status of newly-approved products is uncertain and failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue;

If we are unable to obtain and maintain effective patent rights for our product candidates or any future product candidates, we may not be able to compete effectively in our markets; and

Our future success depends in part upon our ability to retain our Founder, President, and Chief Executive Officer and to attract, retain, and motivate other qualified personnel.

Our Corporate Information

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

We have filed trademark applications with the U.S. Patent and Trademark Office for the marks Ultragenyx and Ultragenyx Pharmaceutical , and we are developing commercial names for our product candidates. This prospectus, and the information incorporated by reference herein, also contains trademarks of others, including Aldurazyme®, Naglazyme®, Kuvan®, Vimizim , Lumizyme® and Myozyme®. We do not intend our use or display of other companies trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

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THE OFFERING

Common stock offered by us	shares
Underwriters option to purchase additional shares	We have granted the underwriters a 30-day option to purchase up to an additional shares of our common stock.
Common stock to be outstanding after this offering	shares (shares if the underwriters exercise their option to purchase additional shares in full)
Use of proceeds	We estimate that the net proceeds to us from this offering will be approximately $117.0 million, or approximately $134.6 million if the underwriters exercise their option to purchase additional shares in full, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us at the assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015. We intend to use the net proceeds of the offering to increase investment in early-stage translational research capabilities, in order to identify and develop potential new products for the pipeline as well as to initiate efforts to establish commercial operations for named-patient sales and potential future marketing authorizations. We may also use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets, though we currently have no specific agreements, commitments, or understandings with respect to any in-licensing or acquisitions. Finally, we may use any remaining proceeds for other ongoing research and development, including funding of late-stage clinical studies, working capital and other general corporate purposes.
Risk factors	You should read the Risk Factors section of this prospectus and our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, incorporated by reference herein, for a discussion of factors to consider carefully 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 31,846,472 shares of common stock outstanding as of September 30, 2014.

The number of shares of our common stock to be outstanding after this offering excludes the following:

2,696,183 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2014 having a weighted-average exercise price of $14.42 per share;

25,000 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2014;

353,459 shares of common stock issuable upon the exercise of outstanding warrants as of September 30, 2014 having a weighted-average exercise price of $3.01 per share;

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1,590,000 shares of common stock reserved for issuance pursuant to future equity awards under our 2014 Incentive Plan as of September 30, 2014, as well as any future increases in the number of shares of our common stock reserved for future issuance under this plan; and

600,000 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, or 2014 ESPP, as of September 30, 2014, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2014 ESPP.

Except as otherwise indicated, all information contained in this prospectus:

assumes that the underwriters do not exercise their option to purchase additional shares; and

assumes no exercise of outstanding options or warrants after September 30, 2014.

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SUMMARY FINANCIAL DATA

The following table summarizes our statements of operations and balance sheet data. We have derived the following statements of operations data for the years ended December 31, 2011, 2012, and 2013 from our audited financial statements incorporated by reference in this prospectus from our Annual Report on Form 10-K for the fiscal year ended December 31, 2013, or our 2013 Annual Report, and we have derived the following statements of operations data for the nine months ended September 30, 2013 and September 30, 2014 and the balance sheet data as of September 30, 2014 from our unaudited interim financial statements incorporated by reference in this prospectus from our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014, or our September 2014 Quarterly Report. You should read this data together with our financial statements and related notes, as well as the information under the captions Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations appearing in our 2013 Annual Report and our September 2014 Quarterly Report, which are incorporated by reference herein. Our historical results are not necessarily indicative of our future results, and results of interim periods are not necessarily indicative of results for the entire year.

	Year Ended December 31,			Nine Months Ended September 30,	
	2011	2012	2013	2013	2014
	(in thousands, except share and per share amounts)			(unaudited)	
Statements of Operations Data:					
Operating expenses:					
Research and development	$ 4,717	$ 12,641	$ 27,829	$ 19,625	$ 32,446
General and administrative	1,844	3,344	4,451	3,130	7,389
Total operating expenses	6,561	15,985	32,280	22,755	39,835
Loss from operations	(6,561)	(15,985)	(32,280)	(22,755)	(39,835)
Interest income	4	1	216	157	413
Interest expense	(270)				
Other expense, net	(22)	(350)	(3,006)	(1,155)	(3,642)
Net loss	$ (6,849)	$ (16,334)	$ (35,070)	$ (23,753)	$ (43,064)
Net loss attributable to common stockholders[1]	$ (7,466)	$ (19,561)	$ (50,289)	$ (31,624)	$ (47,872)
Net loss per share attributable to common stockholders, basic and diluted	$ (4.62)	$ (14.20)	$ (14.87)	$ (9.70)	$ (1.73)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	1,617,384	1,377,207	3,382,489	3,260,484	27,697,137

	As of September 30, 2014	
	Actual	As Adjusted[2][3]
	(in thousands)	
	(unaudited)	
Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 201,194	$ 318,199
Working capital	195,669	312,674
Total assets	210,931	327,936
Accumulated deficit	(122,302)	(122,302)
Total stockholders equity	199,326	316,331

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(1) See (a) Notes 2 and 14 to our audited financial statements included in our 2013 Annual Report incorporated by reference herein and (b) Notes 2 and 11 to our interim financial statements included in our September 2014 Quarterly Report incorporated herein by reference for an explanation of the calculations of our basic and diluted net loss per share attributable to common stockholders.

(2) The as-adjusted balance sheet data reflects the sale of an assumed 2,203,031 shares of common stock offered by us in this offering at an assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) A $1.00 increase (decrease) in the assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, would increase (decrease) the as adjusted amount of each of cash, cash equivalents and short-term investments, working capital, total assets and total stockholders equity by approximately $2.1 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A 100,000 share increase (decrease) in the number of shares offered by us at the assumed public offering price of $56.74 per share would increase (decrease) the as adjusted amount of each of cash, cash equivalents and short-term investments, working capital, total assets and total stockholders equity by approximately $5.3 million after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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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 or incorporated by reference in this prospectus, including the risks and uncertainties discussed under Risk Factors in this prospectus and 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 Related to this Offering

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the as-adjusted book value per share of our tangible assets after subtracting our liabilities. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of $47.45 per share, based on an assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, and our as-adjusted net tangible book value as of September 30, 2014 after giving effect to this offering. For information on how the foregoing amounts were calculated, see Dilution.

This dilution is due to the substantially lower price paid by our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, as of September 30, 2014, we had outstanding 25,000 restricted stock units and options and warrants to purchase 3,049,642 shares of our common stock; the vesting of the restricted stock units and the exercise of any of these options or warrants would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation.

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

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the market price of our common stock could decline. Based upon the number of shares of common stock outstanding as of September 30, 2014, and an assumed offering price per share of $56.74 as of February 2, 2015, upon the closing of this offering we will have outstanding a total of approximately 34,049,503 shares of common stock. Of these shares, the shares of our common stock sold in our public offerings in 2014 (other than any shares purchased by our then-existing investors and directors and officers) are currently freely tradable, and the shares to be sold in this offering, plus any shares sold upon exercise of the underwriters option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering. Morgan Stanley & Co. LLC, Cowen and Company, LLC and Jefferies LLC, however, may, in their sole discretion, permit our officers, directors and stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

Certain holders of shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. See Description of Capital Stock Registration Rights. Registration of these shares under the

Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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We will have broad discretion in the use of the net proceeds to us from this offering; we may not use the offering proceeds that we receive effectively.

Our management will have broad discretion in the application of the net proceeds to us from this offering, including for any of the purposes described in the section entitled Use of Proceeds, and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds to us from this offering, their ultimate use may vary from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds to us from this offering in investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus 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 are forward-looking statements. In some cases, you can identify forward-looking statements by words such as anticipate, believe, contemplate, continue, could, estimate, expect, intend, may, plan, potentia 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 expectations regarding the timing of commencing our clinical studies and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the potential market opportunities for commercializing our product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use;
- estimates of our expenses, future 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 and product candidates;
- the initiation, timing, progress, and results of future preclinical studies 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 product candidates;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contact research organizations, suppliers and distributors;

our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;

our use of proceeds from this offering;

our financial performance and expansion of our organization;

our ability to obtain supply of our product candidates;

developments and projections relating to our competitors and our industry; and

other risks and uncertainties, including those listed in Risk Factors.

Any forward-looking statements in this prospectus reflect our current views with respect to future events or 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 listed under Risk Factors and elsewhere and incorporated by reference in this prospectus. 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.

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This prospectus also contains estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the 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.

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USE OF PROCEEDS

We estimate that the net proceeds to us from the assumed sale of 2,203,031 shares of common stock offered by us in this offering will be approximately $117.0 million, based on an assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately $134.6 million, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each $1.00 increase (decrease) in the assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, would increase (decrease) the net proceeds to us by approximately $2.1 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 100,000 shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately $5.3 million, assuming that the assumed public offering price remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds of the offering to increase investment in early-stage translational research capabilities, in order to identify and develop potential new products for the pipeline as well as to initiate efforts to establish commercial operations for named-patient sales and potential future marketing authorizations. We may also use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets, though we currently have no specific agreements, commitments, or understandings with respect to any in-licensing or acquisitions. Finally, we may use any remaining proceeds for other ongoing research and development, including funding of late-stage clinical studies, working capital and other general corporate purposes.

Our expected use of net proceeds to us from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot predict with complete certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the actual amounts that we will spend on the uses set forth above. Due to the many variables inherent to the development of our product candidates, we cannot currently predict the stage of development we expect the net proceeds to us of this offering to achieve for our clinical studies and product candidates.

The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of preclinical studies, our ongoing clinical studies or clinical studies we may commence in the future and the timing of regulatory submissions. As a result, our management will have broad discretion over the use of the net proceeds to us from this offering.

Pending the use of the proceeds to us from this offering, we intend to invest these proceeds in interest-bearing, investment-grade securities, certificates of deposit, or government securities.

Our operating expenses for the three and nine month periods ended September 30, 2014 were $15.8 million and $39.8 million, respectively. As compared to the three months ended September 30, 2014, operating expenses for the three months ended December 31, 2014 are expected to have been at approximately the same level as, or slightly lower than, operating expenses in the third quarter of 2014. However, we expect that our quarterly and annual operating expenses will accelerate in 2015, as well as further accelerate in 2016, as we advance development of KRN23 in XLH and TIO, proceed through Phase 3 development of rhGUS in MPS 7, progress triheptanoin for LC-FAOD and Glut1, and initiate Phase 3 studies and file for conditional approval in Europe for SA-ER in HIBM. We estimate that, with

our current operating plan, the proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, will fund our activities into 2018.

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PRICE RANGE OF COMMON STOCK

Our common stock has been publicly traded on The NASDAQ Global Select Market under the symbol RARE since January 31, 2014. Prior to that time, there was no public market for our common stock. The following table sets forth the high and low sale prices per share for our common stock on The NASDAQ Global Select Market for the periods indicated:

	High	Low
2014		
First Quarter (beginning January 31, 2014)	$ 69.77	$ 35.15
Second Quarter	$ 60.00	$ 32.02
Third Quarter	$ 60.04	$ 37.77
Fourth Quarter	$ 58.33	$ 38.01
2015		
First Quarter (through February 2, 2015)	$ 59.00	$ 44.27

On February 2, 2015, the last reported sale price of our common stock on The NASDAQ Global Select Market was $56.74 per share. As of January 30, 2015, we had approximately 15 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

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DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. Although we have paid dividends to our holders of preferred stock in the past, including a $4.3 million cash dividend paid in February 2014 in connection with our initial public offering, all dividends were agreed to at the time of the private placement financings. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors or any authorized committee thereof.

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CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term investments and capitalization as of September 30, 2014:

- on an actual basis; and
- on an as-adjusted basis to reflect the issuance and sale by us of an assumed 2,203,031 shares of our common stock in this offering at an assumed public offering price of $56.74 per share, which was the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our financial statements and related notes and the information under the captions Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations, appearing in our 2013 Annual Report and September 2014 Quarterly Report, incorporated by reference in this prospectus. For more details on how you can obtain our Commission reports and other information, you should read the section of the prospectus entitled Where You Can Find More Information.

	As of September 30, 2014	
	Actual	As Adjusted[1]
	(in thousands, except share and per share data)	
	(unaudited)	
Cash, cash equivalents and short-term investments	$ 201,194	$ 318,199
Stockholders equity:		
Preferred stock, par value $0.001 per share 25,000,000 shares authorized; no shares issued or outstanding, actual and as adjusted		
Common stock, par value $0.001 per share 250,000,000 shares authorized; 31,846,472 shares issued and outstanding, actual; 250,000,000 shares authorized, 34,049,503 shares issued and outstanding, as adjusted	32	34
Additional paid-in capital	321,714	438,717
Accumulated other comprehensive loss	(118)	(118)
Accumulated deficit	(122,302)	(122,302)
Total stockholders equity	199,326	316,331
Total capitalization	$ 199,326	$ 316,331

(1) A $1.00 increase (decrease) in the assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, would increase (decrease) the as adjusted amount of each of cash, cash equivalents and short-term investments, additional paid-in capital, total stockholders equity and total capitalization by approximately $2.1 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A 100,000 share increase (decrease) in the number of shares offered by us at the assumed public offering price of $56.74 per share would increase (decrease) the as adjusted amount of each of cash, cash equivalents and short-term investments, additional paid-in capital, total stockholders equity and total capitalization by approximately $5.3 million after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

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The number of shares of common stock issued and outstanding in the table above excludes the following shares as of September 30, 2014:

2,696,183 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2014 having a weighted-average exercise price of $14.42 per share;

25,000 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2014;

353,459 shares of common stock issuable upon the exercise of outstanding warrants as of September 30, 2014 having a weighted-average exercise price of $3.01 per share;

1,590,000 shares of common stock reserved for issuance pursuant to future equity awards under our 2014 Incentive Plan as of September 30, 2014, as well as any future increases in the number of shares of our common stock reserved for future issuance under this plan; and

600,000 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, or 2014 ESPP, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2014 ESPP.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the as-adjusted net tangible book value per share of our common stock immediately after this offering.

Net tangible book value per share is determined by dividing our total tangible assets less our total liabilities by the number of shares of common stock outstanding. Our historical net tangible book value as of September 30, 2014 was approximately $199.3 million, or $6.26 per share.

Dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the as-adjusted net tangible book value per share of common stock immediately after completion of this offering. After giving effect to the sale of an assumed 2,203,031 shares of common stock in this offering by us at an assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as-adjusted net tangible book value as of September 30, 2014 would have been $316.3 million, or $9.29 per share. This represents an immediate increase in net tangible book value of $3.03 per share to existing stockholders and an immediate dilution of $47.45 per share to investors participating in this offering, as illustrated in the following table:

Assumed public offering price per share		$ 56.74
Historical net tangible book value per share as of September 30, 2014	$ 6.26	
Increase in as-adjusted net tangible book value per share attributable to new investors	3.03	
As-adjusted net tangible book value per share after this offering		9.29
Dilution per share to investors participating in this offering		$ 47.45

Each $1.00 increase (decrease) in the assumed public offering price of $56.74 per share, which is the last reported sale price of our common stock on The NASDAQ Global Select Market on February 2, 2015, would increase (decrease) the as adjusted net tangible book value by approximately $2.1 million, or approximately $0.06 per share, and increase (decrease) the dilution per share to new investors by approximately $0.94 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of 100,000 shares in the number of shares offered by us would increase the as adjusted net tangible book value by approximately $5.3 million, or $0.13 per share, and the dilution per share to new investors would be a decrease of approximately $0.13 per share, assuming that the assumed public offering price remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, a decrease of 100,000 shares in the number of shares offered by us would decrease the as adjusted net tangible book value by approximately $5.3 million, or approximately $0.13 per share, and the dilution per share to new investors would be an increase of approximately $0.13 per share, assuming that the assumed public offering price remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

The foregoing calculations exclude the following shares as of September 30, 2014:

2,696,183 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2014 having a weighted-average exercise price of $14.42 per share;

25,000 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2014;

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353,459 shares of common stock issuable upon the exercise of outstanding warrants as of September 30, 2014 having a weighted-average exercise price of $3.01 per share;

1,590,000 shares of common stock reserved for issuance pursuant to future equity awards under our 2014 Incentive Plan as of September 30, 2014, as well as any future increases in the number of shares of our common stock reserved for future issuance under this plan; and

600,000 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, or 2014 ESPP, 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 will experience further dilution if any of our outstanding options or warrants 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.

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DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 250,000,000 shares of common stock, par value $0.001 per share, and 25,000,000 shares of preferred stock, par value $0.001 per share. The following description of our capital stock is intended as a summary only and is qualified in its entirety by reference to our amended and restated certificate of incorporation, and amended and restated by-laws, copies of which are incorporated by reference as exhibits to the registration statement, of which this prospectus forms a part, and to the applicable provisions of the Delaware General Corporation Law.

Common Stock

As of December 31, 2014, there were 31,934,682 shares of our common stock outstanding, held of record by approximately 16 stockholders. Based on shares outstanding as of December 31, 2014, upon completion of this offering, there will be 34,137,713 shares of our common stock outstanding.

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. Except as described below in Anti-Takeover Effects of Delaware Law, Our Certificate of Incorporation and Our By-laws, 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.

Preferred Stock

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. As of December 31, 2014, no shares of preferred stock were outstanding and we have no current plans to issue any shares of preferred stock.

Warrants

As of December 31, 2014, warrants to purchase a total of 324,351 shares of our common stock were outstanding with an exercise price of $3.01 per share. These warrants are exercisable immediately and each expire on the first to occur of (i) the closing date of any reorganization, consolidation or merger of the Company, transfer of all or substantially all of the assets of the Company or any simultaneous sale of more than a majority of the then outstanding securities of the Company other than a mere reincorporation transaction, or (ii) the 10 year anniversary of the date of such warrant which in the case of the outstanding warrants of the Company is June 2020, February 2021 and June 2021, respectively.

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Registration Rights

We are party to an amended and restated investors rights agreement, dated as of December 18, 2012, with certain holders of our common stock. Under the amended and restated investors rights agreement, holders of registrable shares have certain demand registration rights and piggyback registration rights, as described more fully below. These registration rights will terminate (i) on February 5, 2019, which is the fifth anniversary of the closing of our initial public offering, or (ii) after this offering, as to any holder of registrable securities, when such holder holds 1% or less of our common stock and all registrable securities held by such holder can be sold in any 90-day period without registration in compliance with Rule 144.

Demand Registration Rights

Under the amended and restated investors rights agreement, beginning July 29, 2014, which is the date that is 180 days after the effective date of the registration statement for our initial public offering, or 45 days following the effective date of any other Company-initiated registration statement, the holders of at least 50% of the registrable shares (or a lesser percentage if the anticipated aggregate offering price is not less than $10 million) then outstanding can, on not more than two occasions, demand that we file a registration statement or request that their shares be included on a registration statement that we are otherwise filing, in either case, registering the resale of their shares of common stock. We are required to use our best efforts to effect the registration and will pay all registration expenses, other than underwriting discounts and commissions, related to any demand registration. These registration rights are subject to conditions and limitations, including the right, in certain circumstances, of the underwriters of an offering to limit the number of shares included in such registration and our right, in certain circumstances, not to effect a requested registration.

Piggyback Registration Rights

If we propose to register any of our securities under the Securities Act for our own account or the account of any other holder, the significant holders (as defined in the amended and restated investors rights agreement) are entitled to notice of such registration and to request that we include registrable shares for resale on such registration statement, subject to the right of any underwriter to limit the number of shares included in such registration.

We will pay all registration expenses, other than underwriting discounts and commissions, related to any piggyback registration. The amended and restated investors rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders, in the event of misstatements or omissions in the registration statement attributable to us and they are obligated to indemnify us for misstatements or omissions attributable to them.

Anti-Takeover Effects of Delaware Law, our Certificate of Incorporation and Our By-laws

Our certificate of incorporation and by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

In accordance with our certificate of incorporation, our board is divided into three classes serving three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting

from an increase in the size of our board, may only be filled by a resolution of the board.

No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

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Meetings of Stockholders

Our certificate of incorporation and by-laws provide that, subject to any rights of holders of any series of preferred stock, only the board or the chairman of the board may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer s own slate of directors or otherwise attempting to obtain control of our company.

Amendment to By-laws and Certificate of Incorporation

As required by the Delaware General Corporation Law, any amendment of our certificate of incorporation must first be approved by a majority of our board of directors and, if required by law or our certificate of incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to directors, stockholders, the amendment of our by-laws and certificate of incorporation and exclusive jurisdiction of Delaware Courts must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the by-laws, and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment.

Blank Check Preferred Stock

Our certificate of incorporation provides for 25,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a three-year period following the time that this stockholder becomes an interested

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stockholder, unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation s voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may opt out of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or by-laws resulting from a stockholders amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Exclusive Jurisdiction of Certain Actions

Our certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought in our name, actions against our directors, officers and employees for breach of fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware, unless we otherwise consent. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

NASDAQ Global Select Market listing

Our common stock is listed on The NASDAQ Global Select Market under the symbol RARE .

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar s address is 620 15th Avenue, Brooklyn, New York 11219.

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MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to non-U.S. holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or foreign tax laws are not discussed. This discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated under the Code, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or IRS, in effect as of the date of this offering. These authorities may change or be subject to differing interpretations. Any such change may be applied retroactively in a manner that could adversely affect a non-U.S. holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to non-U.S. holders that hold our common stock as a capital asset within the meaning of Section 1221 of the Code (property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a non-U.S. holder s particular circumstances, including the impact of the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to non-U.S. holders subject to particular rules, including, without limitation:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies and other financial institutions;
- brokers, dealers or traders in securities;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes;
- tax-exempt organizations or governmental organizations;

persons deemed to sell our common stock under the constructive sale provisions of the Code;

persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and

tax-qualified retirement plans.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATION PURPOSES ONLY AND IS NOT INTENDED AS TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

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Definition of a Non-U.S. Holder

For purposes of this discussion, a non-U.S. holder is any beneficial owner of our common stock that is neither a U.S. person nor a partnership for United States federal income tax purposes. A U.S. person is any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more United States persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled Dividend Policy, we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions on our common stock, such distributions of cash or property on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder s adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below in the section titled Sale or Other Taxable Disposition.

Subject to the discussions below regarding backup withholding and foreign accounts, dividends paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty). Even if a non-U.S. holder is eligible for a lower treaty rate, dividend payments will generally be subject to withholding at a 30% rate (rather than the lower treaty rate) unless the non-U.S. holder provides a valid IRS Form W-8BEN or W-8BEN-E (or applicable successor form) certifying such holder s qualification for the reduced rate.

Subject to the discussions below regarding backup withholding and foreign accounts, if dividends paid to a non-U.S. holder are effectively connected with the non-U.S. holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such dividends are attributable), the non-U.S. holder will be exempt from U.S. federal withholding tax. To claim the exemption, the non-U.S. holder must furnish to us or our paying agent a valid IRS Form W-8ECI (or applicable successor form), certifying that the dividends are effectively connected with the non-U.S. holder s conduct of a trade or business within the United States.

Any dividends paid on our common stock that are effectively connected with a non-U.S. holder s U.S. trade or business (and, if required by an applicable tax treaty, attributable to a permanent establishment maintained by the

non-U.S. holder in the United States) generally will be subject to U.S. federal income tax on a net income basis in the same manner as if such holder were a U.S. person. A non-U.S. holder that is a corporation also may, under certain circumstances, be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable tax treaty) on any effectively connected dividends that it receives. Non-U.S. holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under a tax treaty. You may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

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Sale or Other Taxable Disposition

Subject to the discussions below regarding backup withholding and foreign accounts, a non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such gain is attributable);
- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or a USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. If a non-U.S. holder is eligible for the benefits of a tax treaty between the United States and its country of residence, any such gain will be subject to U.S. federal income tax in the manner specified by the treaty. To claim the benefit of a treaty, a non-U.S. holder must properly submit an IRS Form W-8BEN (or suitable successor or substitute form). A non-U.S. holder that is a foreign corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on any gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the United States) provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we are not currently and do not anticipate becoming a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our USRPIs relative to the fair market value of our other business assets and our non-U.S. real property interests, there can be no assurance we are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a non-U.S. holder of our common stock will not be subject to U.S. federal income tax if our common stock is regularly traded, as defined by applicable Treasury Regulations, on an established securities market, and such non-U.S. holder owned, actually or constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other disposition or the non-U.S. holder s holding period.

Non-U.S. holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

A non-U.S. holder will not be subject to backup withholding with respect to payments of dividends on our common stock we make to the non-U.S. holder, provided the holder certifies its non-U.S. status, such as by providing a valid IRS Form W-8BEN, W-8ECI, or other applicable IRS Form, or otherwise establishes an exemption. However, information returns will be filed with the IRS in connection with any dividends on our common stock paid to the non-U.S. holder, regardless of whether any tax was actually withheld. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Information reporting and, depending on the circumstances, backup withholding will apply to the proceeds of a sale of our common stock within the United States or conducted through certain U.S.-related financial intermediaries, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder on Form W-8BEN or other applicable form or such owner otherwise establishes an exemption.

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Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder s U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Sections 1471 through 1474 of the Code (FATCA) generally impose a 30% withholding tax on dividends paid on, and the gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution (as defined in the Code) or to a non-financial foreign entity (as defined in the Code) (whether such foreign financial institution or non-financial foreign entity is the beneficial owner or an intermediary), unless (1) in the case of a foreign financial institution, the entity undertakes certain diligence and reporting obligations, (2) in the case of a non-financial foreign entity, the entity either certifies that it does not have any substantial United States owners (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities (as defined in applicable Treasury Regulations), annually report certain information about such accounts, and withhold 30% on payments to non-compliant foreign financial institutions and certain other account holders. Foreign governments may enter into an agreement with the IRS to implement FATCA in a different manner. Under current IRS guidance, these withholding and reporting requirements will apply currently with respect to dividends on the common stock, but will not apply to withholding on gross proceeds on the sale or other taxable disposition of the common stock until January 1, 2017. If you are located in a jurisdiction that has an intergovernmental agreement with the United States governing FATCA, you may be subject to different rules. Prospective investors should consult their tax advisors regarding these withholding provisions.

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UNDERWRITERS

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, the underwriters named below, for whom Morgan Stanley & Co. LLC, Cowen and Company, LLC and Jefferies LLC are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. LLC	
Cowen and Company, LLC	
Jefferies LLC	
Canaccord Genuity Inc.	
JMP Securities LLC	
Robert W. Baird & Co. Incorporated	
SunTrust Robinson Humphrey, Inc.	
Wedbush Securities Inc.	
Total	

The underwriters and the representatives are collectively referred to as the underwriters and the representatives, respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus supplement are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus supplement if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters option to purchase additional shares described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus supplement and part to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to $18,750,000 of additional shares of common stock at the public offering price listed on the cover page of this prospectus supplement, less underwriting discounts and commissions. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter s name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase up to an additional $18,750,000 of shares of common stock.

	Per Share	Total No Exercise	Total Full Exercise
Public offering price	$	$	$
Underwriting discounts and commissions	$	$	$
Proceeds, before expenses, to us	$	$	$

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The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately $495,000. We have agreed to reimburse the underwriters for expense relating to clearance of this offering with the Financial Industry Regulatory Authority up to $25,000.

Our common stock is listed on The NASDAQ Global Select Market under the symbol RARE .

We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act, relating to, any shares of our common stock or any securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of our common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of our common stock or such other securities, in cash or otherwise), in each case without the prior written consent of Morgan Stanley & Co. LLC, Cowen and Company, LLC and Jefferies LLC for a period of 90 days after the date of this prospectus, other than (i) the shares of our common stock to be sold hereunder, (ii) any shares of our common stock issued upon the vesting of restricted stock units or the exercise of options granted under our existing management incentive plans or warrants described as outstanding in the registration statement of which this prospectus forms a part, (iii) any options and other awards granted under an equity incentive plan described in the registration statement of which this prospectus forms a part, (iv) our filing of any registration statement on Form S-8 or a successor form thereto relating to an equity incentive plan described in the registration statement of which this prospectus forms a part, and (v) shares of common stock or other securities issued in connection with a transaction with an unaffiliated third party that includes a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or acquisition of not less than a majority or controlling portion of the equity of another entity, provided that (x) the aggregate number of shares issued pursuant to this clause (v) shall not exceed five percent (5%) of the total number of outstanding shares of common stock immediately following the issuance and sale of the shares of common stock in this offering and (y) the recipient of any such shares of common stock and securities issued pursuant to this clause (v) during the 90-day restricted period described above shall enter into a lock-up agreement.

Our directors, executive officers and certain shareholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 90 days after the date of this prospectus, may not, without the prior written consent of Morgan Stanley & Co. LLC, Cowen and Company, LLC and Jefferies LLC, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers and shareholders in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge or disposition, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. The restrictions described in the immediately preceding paragraph to do not apply to:

transfers or dispositions of shares of common stock (or any security convertible into or exercisable or exchangeable for common stock):

as a bona fide gift;

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to any trust for the direct or indirect benefit of the party subject to the lock-up restrictions or the immediate family of such person;

to any corporation, partnership, limited liability company, investment fund or other entity controlled or managed, or under common control or management by the party subject to the lock-up restrictions or the immediate family of such person;

by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the party subject to the lockup restrictions; or

as distributions to partners, members or stockholders of the party subject to the lock-up restrictions, *provided* that in the case of any transfer or distribution pursuant to the above five subclauses, (i) each donee or distributee shall sign and deliver a lock-up letter substantially in the form executed by the party subject to the lock-up restrictions and (ii) no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5);

sales or transfers of common stock made pursuant to a trading plan pursuant to Rule 10b5-1 under the Exchange Act, or Rule 10b5-1, that has been entered into prior to the date of this prospectus, provided that to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made by or on behalf of the party subject to such lock-up restrictions regarding any such sales or transfers, such announcement or filing shall include a statement to the effect that the sale or transfer was made pursuant to a trading plan pursuant to Rule 10b5-1;

the establishment of a trading plan pursuant to Rule 10b5-1 for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) no filing under the Exchange Act or other public announcement shall be required or voluntarily made by or on behalf of the party subject to the lock-up restrictions regarding the establishment of such plan;

the exercise of options to purchase shares of common stock granted under any stock incentive plan or stock purchase plan of the Company, provided that the underlying shares shall continue to be subject to the restrictions on transfer set forth in the lock-up agreement and provided further that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5);

the exercise (whether for cash, cashless, or net exercise) of warrants to purchase shares of common stock (or any security convertible into or exercisable or exchangeable for common stock), provided that the underlying shares shall continue to be subject to the lock-up restrictions and provided further that, other than in respect of warrants that will expire or automatically exercise by their terms in connection with this offering, no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made during the restricted

period (other than a filing on Form 5);

the transfer of shares of common stock (or any security convertible into common stock) to the Company or sold in connection with a vesting event of the Company s securities or upon the exercise of options to purchase the Company s securities, on a cashless or net exercise basis or to cover tax withholding obligations of the party subject to the lock-up restrictions in connection with such vesting or exercise provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made during the restricted period (other than a filing on Form 5);

the transfer or disposition of the shares of common stock (or any security convertible into or exercisable or exchangeable for common stock) held by the party subject to the lock-up restrictions that occurs by operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement provided that each transferee shall sign and deliver a lock-up letter substantially in the form executed by the party subject to the lock-up restrictions;

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the transfer of shares of common stock (or any security convertible into or exercisable or exchangeable for common stock) pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction made to all holders of the common stock involving a change of control of the Company, provided that in the event that the tender offer, merger, consolidation or other such transaction is not completed, the common stock owned by the party subject to the lock-up restrictions shall remain subject to such restrictions; or

transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares, provided that no filing under Section 16(a) of the Exchange Act is required or voluntarily made in connection with subsequent sales of the common stock or other securities acquired in such open market transactions (other than a filing on Form 5);

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option. The underwriters can close out a covered short sale by exercising the option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option. The underwriters may also sell shares in excess of the option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus supplement in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and

securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research

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views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (FSMA) received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

Japan

No registration pursuant to Article 4, paragraph 1 of the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) (the FIEL) has been made or will be made with respect to the solicitation of the application for the acquisition of the shares of common stock.

Accordingly, the shares of common stock have not been, directly or indirectly, offered or sold and will not be, directly or indirectly, offered or sold in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the

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laws of Japan) or to others for re-offering or re-sale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan except pursuant to an exemption from the registration requirements, and otherwise in compliance with, the FIEL and the other applicable laws and regulations of Japan.

For Qualified Institutional Investors (QII)

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a QII only private placement or a QII only secondary distribution (each as described in Paragraph 1, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred to QIIs.

For Non-QII Investors

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a small number private placement or a small number private secondary distribution (each as is described in Paragraph 4, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred en bloc without subdivision to a single investor.

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LEGAL MATTERS

Gibson, Dunn & Crutcher LLP, San Francisco, California will pass upon the validity of the shares of common stock offered hereby. Certain legal matters in connection with this offering will be passed upon for the underwriters by Latham & Watkins LLP, Costa Mesa, California.

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, 2013, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the 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.

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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.

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 2, 2015 was $56.74 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 4 OF THIS PROSPECTUS AS WELL AS THOSE IN ANY SIMILAR SECTION 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 upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is February 3, 2015

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We have not authorized anyone to provide you with information other than that contained in this prospectus 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.

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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, 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 separately or in units, 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 to this prospectus 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 related 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 or a selling stockholder 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 similar references refer to Ultragenyx Pharmaceutical Inc.; 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 have filed trademark applications with the U.S. Patent and Trademark Office for the marks Ultragenyx and Ultragenyx Pharmaceutical , and we are developing commercial names for our product candidates. This prospectus, and the information incorporated by reference herein, also contains trademarks of others, including Aldurazyme®, Naglazyme®, Kuvan®, Vimizim , Lumizyme® and Myozyme®. We do not intend our use or display of other companies trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

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ABOUT ULTRAGENYX PHARMACEUTICAL INC.

Ultragenyx is a clinical-stage biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. We target diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies. Since our inception in 2010, we have in-licensed potential treatments for multiple rare genetic disorders. Our strategy, which is predicated upon time- and cost-efficient drug development, allows us to pursue multiple programs in parallel with the goal of delivering safe and effective therapies to patients with the utmost urgency.

Our current pipeline consists of two product categories: biologics, including a monoclonal antibody and enzyme replacement therapies; and small-molecule substrate replacement therapies. Enzymes are proteins that the body uses to process materials needed for normal cellular function, and substrates are the materials upon which enzymes act. When enzymes or substrates are missing, the body is unable to perform its normal cellular functions, often leading to significant clinical disease. Several of our therapies are intended to replace deficient enzymes or substrates.

Our biologics pipeline includes the following product candidates:

KRN23, or UX023, is an antibody targeting fibroblast growth factor 23, or FGF23, intended for the treatment of X-linked hypophosphatemia, or XLH, a rare genetic disease that impairs bone growth. We are developing KRN23 pursuant to our collaboration with Kyowa Hakko Kirin Co., Ltd., or KHK. KHK has completed one Phase 1 study, one Phase 1/2 study, and one longer-term Phase 1/2 study of KRN23 in adults with XLH. We initiated a Phase 2 pediatric study in July 2014 that has been fully enrolled. We also expect to initiate a Phase 2b clinical study in adults with XLH in 2015.

KRN23 is also intended for the treatment of tumor-induced osteomalacia, or TIO. TIO results from typically benign tumors that produce excess levels of FGF23, which can lead to severe osteomalacia, bone fractures, bone and muscle pain, and muscle weakness. We intend to initiate a Phase 2 study of KRN23 in six adult TIO patients in the first half of 2015.

rhGUS, or UX003, is an enzyme replacement therapy we are developing for the treatment of mucopolysaccharidosis 7, or MPS 7, a rare lysosomal storage disease that often leads to multi-system disease, pervasive skeletal disease, and early death. We initiated a Phase 3 clinical study in December 2014.

rhPPCA, or UX004, is an enzyme replacement therapy in preclinical development for galactosialidosis, a rare lysosomal storage disease that can cause multi-system clinical disease similar to MPS 7, including an enlarged liver, joint disease, abnormal bone development, short stature, and early death. We continue preclinical development of rhPPCA.

Our substrate replacement therapy pipeline includes the following product candidates in development for three diseases:

Triheptanoin, or UX007, is a synthetic triglyceride with a specifically designed chemical composition being studied as an energy substrate replacement therapy in an international open-label Phase 2 study for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD. LC-FAOD is a set of rare metabolic diseases caused by the inability to convert fat into energy, which leads to low blood sugar, muscle rupture, and heart and liver disease.

Triheptanoin is also in a Phase 2 study for the treatment of glucose transporter type-1 deficiency syndrome, or Glut1 DS, a rare metabolic disease of brain energy deficiency that is characterized by seizures, developmental delay, and movement disorder.

SA-ER, or UX001, is an extended-release form of sialic acid in a Phase 2 extension study for the treatment of hereditary inclusion body myopathy, or HIBM, a neuromuscular disorder that causes

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muscle weakness and wasting. We plan to initiate a Phase 3 clinical study by mid-2015 and intend to file a Marketing Authorization Application seeking conditional approval from the European Medicines Agency for the use of SA-ER in the treatment of HIBM in the second half of 2015.

Ultragenyx was incorporated in California in April 2010 and was reincorporated in Delaware in June 2011. Our principal executive offices are located at 60 Leveroni Court, Novato, California 94949, and our telephone number is (415) 483-8800. Our web site 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 web site and in our periodic and current reports filed with the SEC. Copies of our current and periodic reports filed with the SEC are available at the SEC Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549, and online at *www.sec.gov* and our web site 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.

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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 to this prospectus as well as in 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 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 are forward-looking statements. In some cases, you can identify forward-looking statements by words such as anticipate, believe, contemplate, continue, could, estimate, expect, intend, may, plan, potentia 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 expectations regarding the timing of commencing our clinical studies and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the potential market opportunities for commercializing our product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use;
- estimates of our expense, future 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 and product candidates;

the initiation, timing, progress, and results of future preclinical studies 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 product candidates;

our ability to maintain and establish collaborations or obtain additional funding;

our ability to maintain and establish relationships with third parties, such as contact research organizations, suppliers and distributors;

our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;

our use of proceeds under this offering;

our financial performance and expansion of our organization;

our ability to obtain supply of our product candidates;

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developments and projections relating to our competitors and our industry; and

other risks and uncertainties.

Any forward-looking statements in this prospectus 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 listed under the section entitled Risk Factors and discussed elsewhere in this prospectus. 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 also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the 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.

RATIO OF EARNINGS TO FIXED CHARGES

Our ratio of earnings to fixed charges for recently completed fiscal years and any required interim periods will be specified in a prospectus supplement or in a document that we file with the SEC and incorporate by reference in the future.

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 separately or in units, 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 such 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

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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 31,934,682 shares were issued and outstanding as of December 31, 2014.

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. The transfer agent and registrar s address is 620 15th Avenue, Brooklyn, New York 11219.

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, par value $0.001 per share, 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.

No shares of preferred stock were issued and outstanding as of December 31, 2014.

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 and any free writing prospectus 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. We may issue debt securities from time to time, in one or more series. The paragraphs below describe the general terms and provisions of the debt securities we may offer under this prospectus. 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.

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 that will govern debt securities that we may issue, or indicated which material provisions will be described in the related prospectus supplement. The

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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 applicable 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 depositary 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 pursuant to the terms of the indenture. 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.

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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 court 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.

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.

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Modification, Amendment, Supplement and Waiver

Without notice to or the consent of any holder of any debt security, we and the trustee may modify, 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;

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 modify, amend, supplement or waive 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 modified, amended, supplemented or waived, a modification, amendment, supplement or waiver may not:

reduce the amount of debt securities of such series whose holders must consent to a modification, 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;

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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 interest, if any, on and the principal of 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 interest, if any, on and the principal of 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 of 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.

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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 the trustee 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 and any free writing prospectus 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.

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If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement or related free writing prospectus, 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.

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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. We may use underwriters with whom we have a material relationship. We will describe in the applicable prospectus supplement, naming the underwriter and the nature of any such relationship.

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 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.

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. Certain legal matters in connection with securities being offered hereby will be passed upon by counsel for any underwriters, dealers or agents as may be specified in the applicable prospectus supplement.

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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, 2013, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the 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, 2013;

2. Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014, June 30, 2014 and September 30, 2014;

3. Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on May 23, 2014;

4. Our Current Reports on Form 8-K filed with the SEC on February 5, 2014, February 25, 2014, July 16, 2014, August 14, 2014 and August 21, 2014; and

5. 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, Suite 200, 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.

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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*. You may also read and copy, at prescribed rates, any document we file with the SEC at the Public Reference Room of the SEC located at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at (800) SEC-0330 for further information on the SEC s Public Reference Rooms.

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$125,000,000

Common Stock

Prospectus Supplement

Morgan Stanley **Cowen and Company** **Jefferies**

Baird **Canaccord Genuity** **JMP Securities**

SunTrust Robinson Humphrey **Wedbush PacGrow Life Sciences**

February , 2015