

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2015

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission File No. 001-36276

**Ultragenyx Pharmaceutical Inc.**

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of  
incorporation or organization)

27-2546083

(I.R.S. Employer Identification No.)

60 Leveroni Court

Novato, California

(Address of principal executive offices)

94949

(Zip Code)

(415) 483-8800

(Registrant's telephone number, including area code)

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

Title of Each Class  
Common Stock, \$0.001 par value

Name of Each Exchange on Which Registered  
The NASDAQ Global Select Market

Securities registered pursuant to Section 12(g) of the Act: None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES  NO

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15 (d) of the Act. YES  NO

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES  NO

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). YES  NO

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

(Do not check if a smaller reporting company)

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES  NO

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Company as of June 30, 2015 was approximately \$2.3 billion, based upon the closing price on The NASDAQ Global Select Market reported for such date. Shares of common stock held by each officer and director and by each person who is known to own 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates of the Company. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 19, 2016, the Company had 38,979,564 shares of common stock issued and outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive Proxy Statement relating to its 2016 Annual Meeting of Stockholders, to be held on or about June 9, 2016, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

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## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements made in this Annual Report on Form 10-K that are not statements of historical information are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We have made these statements in reliance on the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements are subject to certain risks and uncertainties, which could cause actual results to differ materially from those projected or anticipated. Although we believe our assumptions underlying our forward-looking statements are reasonable as of the date of this report, we cannot assure you that the forward-looking statements set out in this report will prove to be accurate. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words or other comparable terminology. Some of the factors that could cause our actual results to differ materially from our expectations or beliefs are disclosed under the caption “Risk Factors,” as well as other sections of this report that include, without limitation: our capital resources, commercial market estimates, safety of our product candidates, the results of clinical trials, future development efforts, patent protection, effects of healthcare reform, reliance on third parties, and other risks set forth below. All forward-looking statements speak only as of the date on which they are made and we disclaim any intent to update forward-looking statements to reflect subsequent developments or actual results. Except as required by law, we assume no obligation to update any forward-looking statements publicly, or to revise any forward-looking statement to reflect events or developments occurring after the date of this report, even if new information becomes available in the future. Thus, you should not assume that our silence over time means that actual events are bearing out as previously expressed or implied in any such forward-looking statement.

This Annual Report on Form 10-K 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.

**Item 1. Business**

**Overview**

We are a clinical-stage biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of serious rare and ultra-rare genetic diseases. We target diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no currently 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 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 highly targeted due to the relatively small number of specialists who treat patients with rare and ultra-rare diseases. At this time, however, we have no products that are approved for sale.

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

We were founded in April 2010 by our current President and Chief Executive Officer, Emil Kakkis, M.D., Ph.D., who is the former Chief Medical Officer of BioMarin Pharmaceutical Inc. 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 genetic diseases.

**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, or EU, and select international markets, with the goal of becoming a leading rare disease biotechnology company. The critical components of our business strategy include the following:

- **Focus on rare and ultra-rare diseases with significant unmet medical need and clear biology.** There are numerous rare and ultra-rare genetic diseases that currently have no approved drug therapy and for which no therapies are currently in development. Patients suffering from these diseases often have a high unmet medical need with significant morbidity and/or mortality. We are focused on developing and commercializing therapies for multiple such indications with the utmost urgency. We also focus on diseases that have biology that is well understood. For example, several of our product candidates are replacement therapies for a single deficient enzyme or substrate in the body. We believe that developing drugs that directly impact known disease pathways will increase the probability of success of our development programs.
- **Leverage our experience and relationships to in-license promising product candidates.** Our management team has strong relationships with key opinion leaders in the genetic field, as well as a history of success in the development and commercialization of therapies for rare and ultra-rare genetic diseases. Accordingly, we enjoy unique access to many in-licensing opportunities. All of our current clinical product candidates are in-licensed from academic institutions or derived from partnerships with other pharmaceutical companies. We believe these parties have agreed to license product candidates to us because they are confident in our team's drug development capabilities and experience in bringing rare disease therapies to market. Because we typically in-license product candidates that require translational or clinical research, we do not invest any capital in basic research, which can be expensive and time-consuming.
- **Focus on excellent, rapid, and efficient clinical and regulatory execution on multiple programs in parallel.** We believe that building a successful and sustainable rare disease-focused company requires very specific expertise in the areas of patient identification, clinical study design and conduct, and regulatory strategy. We have assembled a team with a successful track record in managing global clinical development activities in an efficient manner and with multinational experience in obtaining regulatory approvals for rare disease products. Clinical studies for rare and ultra-rare diseases can often be smaller in size, fewer in number, and less expensive than those for larger market indications. Development of multiple programs in rare diseases also generates organizational efficiencies and economies of scale. We also seek to manage our fixed cost structure by outsourcing manufacturing of our product candidates. As a result of these efficiencies, we can feasibly develop multiple clinical-stage product candidates in parallel, resulting in a more diversified portfolio that provides multiple opportunities to create value.

**Seek to retain global commercialization rights to product candidates.** We intend to seek and retain global commercialization rights to our product candidates whenever possible to maximize the potential value of our product portfolio. Our plan is to establish our own commercial organization in major pharmaceutical markets and develop a network of third-party distributors in smaller markets. We believe this commercial organization can be highly targeted due to the relatively small number of specialists who typically treat patients with the diseases to be addressed by our product candidates. As a result, we do not expect that we will require pharmaceutical partners for commercialization of our product candidates in major markets, although we may consider partnering for certain territories or indications or for other strategic purposes.

## Clinical Product Candidates

Our current clinical-stage 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.

The following table summarizes our current clinical-stage product candidate pipeline:

Candidate	Description	Indication	Phase 1	Phase 2	Phase 3	Status / Anticipated milestones in 2016	Ultragenyx commercial rights
<b>Biologics</b>							
KRN23 (UX023)	Anti-FGF23 monoclonal antibody	XLH				<ul style="list-style-type: none"> <li>40 week data (n=52) from pediatric Phase 2 study in mid-2016</li> <li>Initiate pediatric Phase 3 study in mid-2016</li> <li>Conditional MAA filing in the second half of 2016</li> </ul>	<ul style="list-style-type: none"> <li>U.S. and Canada Joint with KHK (profit share)</li> <li>Mexico, Central and South America</li> </ul>
KRN23 (UX023)	Anti-FGF23 monoclonal antibody	TIO				<ul style="list-style-type: none"> <li>Interim data from Phase 2 study in the first half of 2016</li> </ul>	<ul style="list-style-type: none"> <li>U.S. and Canada Joint with KHK (profit share)</li> <li>Mexico, Central and South America</li> </ul>
rhGUS (UX003)	Enzyme replacement	MPS 7				<ul style="list-style-type: none"> <li>Data from Phase 3 study in mid-2016</li> </ul>	<ul style="list-style-type: none"> <li>Worldwide</li> </ul>
<b>Substrate replacement therapies</b>							
UX007 Triheptanoin	Substrate replacement	LC-FAOD				<ul style="list-style-type: none"> <li>78 week data from Phase 2 study in the second half of 2016</li> </ul>	<ul style="list-style-type: none"> <li>Worldwide</li> </ul>
UX007 Triheptanoin	Substrate replacement	Glut1 DS				<ul style="list-style-type: none"> <li>Initiate movement disorders Phase 3 study in the second half of 2016</li> <li>Data from the Phase 2 seizure study in the second half of 2016</li> </ul>	<ul style="list-style-type: none"> <li>Worldwide</li> </ul>
Ace-ER (UX001; formerly SA-ER)	Substrate replacement	GNE Myopathy (Formerly HIBM)				<ul style="list-style-type: none"> <li>CHMP opinion on conditional MAA in Europe in the second half of 2016</li> </ul>	<ul style="list-style-type: none"> <li>Worldwide (excluding Japan and certain other Asian territories)</li> </ul>

### 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 fibroblast growth factor 23, or 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, and muscle weakness. There is no approved drug therapy or treatment for the underlying cause of XLH. Most patients are managed using frequently dosed oral phosphate replacement and vitamin D therapy, which can lead to 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 Kyowa Hakko Kirin Co., Ltd., or KHK, as amended in August 2015, to jointly develop and commercialize KRN23. 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.

Results from a four-month Phase 1/2 study in 28 adult XLH patients and subsequent twelve-month Phase 1/2 study of KRN23 in 22 patients were presented at the 2014 ICE/ENDO joint meeting of The Endocrine Society and the International Congress on Endocrinology in June 2014 and ASBMR Annual Meeting in September 2014, respectively.

In July 2014, we announced the first patient screened and enrolled in the Phase 2 pediatric study of KRN23 in patients aged 5 to 12 with XLH. The study consists of a 16-week individual dose-titration period followed by a 48-week treatment period, for a total of 64 weeks. Patients were 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 were allowed to continue to receive dose increases in order to reach the individually-optimized dose of KRN23 on a monthly or biweekly basis for the 48-week treatment period. In late 2014, we completed enrollment of 36 patients. Based on positive 16 week data, we decided to enroll an additional 16 patient cohort with patients that had more severe disease at baseline (based on their Thacher Rickets Severity Scoring System knee score >1.5). Patients for the Phase 2 study were enrolled at nine global centers of excellence in XLH. 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 are also assessing 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.

In December 2015 we released interim data through 40 weeks from the first 36 patients in this study. Thirty five of 36 patients had previously been on standard of care (oral phosphate/vitamin D therapy) for an average of 6.6 years (range: 0 - 11.7 years). Patient demographics were well balanced between the biweekly (n=18) and monthly (n=18) dose groups. Rickets were evaluated via two scoring systems – the Thacher Rickets Severity Scoring System (RSS) and the Radiographic Global Impression of Change (RGI-C). A subset of patients (n=18; 9 dosed biweekly and 9 dosed monthly) were pre-specified as having high rickets severity (greater bone disease) if their baseline total RSS scores were  $\geq 1.5$ . For the responder analysis using total RSS, responders were pre-defined as those patients who had baseline total RSS scores > 1.0 and had 1.0 or more reduction at Week 40 which is considered a significant improvement.

Overall, in all patients (n=36), the mean total RSS score decreased from 1.43 at baseline to 1.00 at 40 weeks (-0.43; 30% reduction; p=0.0076), and 61% of the patients (14/23) were responders. In all the high severity patients (n=18), the mean total rickets score decreased from 2.31 at baseline to 1.22 at 40 weeks (-1.08; 47% reduction; p<0.0001), and 72% of these patients were responders (13/18). In patients who were dosed bi-weekly (n=18), the mean total RSS score decreased from 1.53 at baseline to 0.86 at 40 weeks (-0.67 points; 44% reduction; p=0.0126), and 75% of the patients (9/12) were responders. In the high severity patients who were dosed bi-weekly (n=9), the mean total rickets score decreased from 2.44 at baseline to 1.00 at 40 weeks (-1.44 points; 59% reduction; p<0.0001), and 89% of these patients were responders (8/9). In patients who were dosed monthly (n=18), the mean total rickets score decreased from 1.33 at baseline to 1.14 at 40 weeks (-0.19 points; 14% reduction), and 46% of the patients (5/11) were responders. In the high severity patients who were dosed monthly (n=9), the mean total RSS score decreased from 2.17 at baseline to 1.44 at 40 weeks (-0.72; 33% reduction) and 56% of these patients (5/9) were responders.

Overall, all patients (n=36) experienced a mean improvement in RGI-C score of +1.38 (p<0.0001) and those patients who were severe (n=18) experienced a mean improvement of +1.85 (p<0.0001) at 40 weeks. Within the high severity subset, 67% (12/18) experienced substantial healing (score >2). Patients who were dosed bi-weekly (n=18) experienced a mean improvement in RGI-C score of +1.56 (p<0.0001). Those patients with high severity rickets (n=9) experienced a mean improvement of +2.00 (p<0.0001) at 40 weeks (substantial healing) and 89% (8/9) experienced substantial healing (score >2). Patients who were dosed monthly (n=18) experienced a mean improvement in RGI-C score of +1.20. The patients with high severity rickets (n=9) experienced a mean improvement of +1.70 at 40 weeks and 44% (4/9) experienced substantial healing (score >2).

Patients with walking impairment at baseline (defined by < 80% predicted normal walk distance in the six minute walk test, or 6MWT; n=14) achieved a mean increase of 80 meters (an approximate 20% increase from baseline) at week 40. Additionally, high and low severity patients with walking impairments at baseline also experienced a mean improvement in meters walked at week 40. Functional disability scores were measured with the Pediatric Orthopedic Society North America/Pediatric Outcome Data Collection Instrument (POSNA/PODCI). When evaluating the Global score of all five domains in those patients with substantial impairment at baseline (n=15) or with severe rickets at baseline (n=18), a substantial mean improvement was observed of about one standard deviation or greater in both dose groups. The Pain/Comfort and Sports/Physical Functioning domains were the most affected at baseline and also substantially improved in these severely affected subjects treated in both dose groups.

The most common treatment-related adverse event reported by preferred term was injection site reaction in 39% of patients. All of these reactions were considered mild. All other treatment-related adverse events were considered mild. There was one serious adverse event considered possibly treatment-related. This was a patient with fever and muscle pain who improved without

complication and is still in the trial. There have been no deaths or discontinuations from the study for any reason. No clinically meaningful changes were observed in mean serum calcium, urinary calcium and in serum intact parathyroid hormone. None of the patients had serum phosphorus levels above the upper limit of normal at any time point. No clinically significant changes were observed in renal ultrasounds pre- and post-treatment. All patients demonstrated increases in serum phosphorus that were consistent with what had been observed previously reaching the low normal or just below normal range. Across both dose groups there were mean increases in both the renal phosphate reabsorption (TmP/GFR) and in serum 1,25 dihydroxy vitamin D levels through 40 weeks of treatment.

Additional data from the pediatric Phase 2 study (40 week data from all 52 patients) are expected in the second half of 2016. We also expect to have 64 week data, including height-growth velocity, from a subset of patients in the second half of 2016. We and our partner, KHK, plan to file for Conditional Marketing Authorization in the EU around the end of 2016 based on these data. In addition, we plan to proceed with a pediatric Phase 3 study in mid-2016. The study will likely utilize RGI-C as the primary endpoint and would include a standard of care reference arm. This study is expected to be required for potential approval in the US and could also serve as a confirmatory study in the EU if a conditional marketing authorization were granted.

We are also continuing to develop KRN23 in adults with XLH. We have initiated a long-term, open-label Phase 2b extension study of KRN23 in adult XLH patients who had previously participated in the studies conducted by KHK. In December 2015 we initiated a Phase 3 study of KRN23 for the treatment of adults with XLH. The Phase 3 study is an international, randomized, double-blind, placebo-controlled clinical study that will assess the efficacy and safety of monthly KRN23 at 24 weeks in approximately 120 adult XLH patients. The primary endpoint of the study will be serum phosphorus levels through 24 weeks and the key secondary endpoint is the Brief Pain Inventory Question 3 (pain at its worst in the last 24 hours) at Week 24. Other secondary endpoints include patient reported outcomes assessing skeletal pain, stiffness, fatigue, motor function, and quality of life in these patients. A 48-week open-label bone quality study in approximately ten adult XLH patients evaluating the potential impact of KRN23 on the underlying osteomalacia via bone biopsy is currently enrolling patients.

### ***KRN23 (UX023) for the treatment of TIO***

We are also developing KRN23 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 are enrolling patients in an open-label, proof of concept Phase 2 clinical study. Interim data from the Phase 2 study are expected in the first half of 2016.

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 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.

### ***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. 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 of rhGUS every other week in three patients with MPS 7. Results from the 12-week analysis evaluating 2 mg/kg of rhGUS every other week were presented in September 2014 at the Society for the Study of Inborn Errors of Metabolism, or SSIEM, Annual Symposium and showed a decline in urinary glycosaminoglycans, or GAG excretion of approximately 40-50% from baseline. After the initial 12 weeks, the study entered a dose-exploration phase in which patients were treated with a lower and then higher dose of rhGUS. The 36-week results, which were presented in February 2015 at the Annual WORLD Symposium, showed a greater change in urinary GAG excretion at the higher 4 mg/kg dose of rhGUS, with a mean urinary GAG reduction of approximately 60%.

Sustained decreases in liver size were observed in the two patients who had enlarged livers at baseline, and an improvement in pulmonary function was observed in the one patient who was able to perform the evaluations. Improvements were also observed in the MPS Health Assessment Questionnaire measure of functional capabilities and in the Physician Global Impression of Change scale of overall health status in this open-label study.

No serious adverse events or infusion-associated reactions were observed in the study. The most common adverse events were consistent with the symptoms of MPS 7 or related to intravenous administration of the investigational therapy, including respiratory disorders, infections, and arthralgia.

We initiated a Phase 3 global, randomized, placebo-controlled, blind-start clinical study in December 2014. The Phase 3 study is assessing 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 study 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 Phase 3 study fully enrolled in June 2015, and data are expected in mid-2016.

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 is also evaluating as secondary endpoints 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.

We have obtained positive feedback from the United States Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, regarding the design of the Phase 3 study. The FDA stated that their evaluation of the pivotal Phase 3 study will be based on the totality of the data on a patient-by-patient basis and advised against the declaration of a primary endpoint. The EMA has agreed that approval under exceptional circumstances could be possible based upon a single positive placebo-controlled pivotal study in approximately 12 patients using 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.

In August 2015 we initiated a study of rhGUS in MPS 7 patients under the age of five years, including potentially younger infants born with hydrops fetalis. These hydropic infants can die within a few months to one year of birth, but enzyme replacement therapy might be able to reduce GAG storage and improve health in these patients. The Phase 2 open-label study will assess the safety, tolerability, and efficacy of rhGUS in up to seven pediatric patients under five years old.

We are also supplying rhGUS to investigators who are treating patients under emergency investigational new drug, or eIND, applications and other expanded access programs. Results following 24 weeks of treatment of the first eIND patient were announced in September 2014 and published in *Molecular Genetics and Metabolism* in February 2015.

### ***UX007 for the treatment of LC-FAOD***

We are developing UX007 for oral administration intended as a substrate replacement therapy for patients with long-chain fatty acid oxidation disorders, or LC-FAOD. UX007 is a purified, pharmaceutical-grade form of triheptanoin, a specially designed synthetic triglyceride compound, created via a multi-step chemical process. UX007 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 over a decade in more than a hundred human subjects affected by a variety of diseases. Multiple investigator-sponsored open-label studies suggest clinical improvements with triheptanoin treatment, even for patients who were on standard of care. We presented data at the International Conference of Inborn Errors of Metabolism, or ICIEM, in August 2013 from a retrospective medical record review study assessing the clinical outcome of triheptanoin treatment on LC-FAOD subjects who had 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. 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 prospective randomized controlled study.

In September 2015, case reports from five infants with moderate or severe cardiomyopathy due to LC-FAOD were presented at the SSIEM Annual Symposium. While on the standard of care medium-chain triglyceride, or MCT, oil, the patients were hospitalized with heart failure that required cardiac support and, in some cases, resuscitation. The patients discontinued MCT oil and then began to receive triheptanoin on an expanded access basis. In patients with known ejection fraction, or EF, values before and after treatment ( $n=4$ ) the mean EF prior to treatment with triheptanoin was 32% (range: 21% to 44%) and after treatment at last assessment was 66% (range: 55% to 71%). The most common adverse events were gastrointestinal distress, including loose stools. One patient discontinued treatment after approximately 14 weeks due to gastrointestinal symptoms. No other significant tolerance issues or treatment-related adverse events were reported. Four of the patients continue to receive triheptanoin. These data are from an expanded access program and are based on open-label uncontrolled treatment, which limits definitive conclusions about efficacy and safety.

In October 2015, we reported interim data on the acute effects of UX007 that was being evaluated in a Phase 2 study in LC-FAOD patients. The study was single-arm open-label and evaluated 29 pediatric and adult patients across three main symptom groups (musculoskeletal, liver/hypoglycemia, and cardiac). Patients needed to have moderate to severe FAOD with significant disease in at least one of these domains or a frequent medical events history in order to enroll. The study began with a four-week run-in period to assess baseline data while on the standard of care therapy including MCT oil, if applicable. Patients on MCT oil then discontinued it and UX007 was titrated to a target dose of 25-35% of total daily caloric intake. Patients were followed to evaluate the effects of UX007 treatment over 24 weeks on several endpoints, including cycle ergometry performance, 12-minute walk test, liver disease/hypoglycemia, cardiac disease, and quality of life. The 24-week analysis mainly evaluated the acute effects of UX007 on the musculoskeletal aspects of the disease. Patients who opted to continue will be treated for a total of 78 weeks, and rates of major medical events, such as rhabdomyolysis, hypoglycemia and cardiac events, will be monitored and compared to rates for the two years prior to treatment with UX007. The study planned to evaluate the safety and tolerability of UX007 and to determine both the appropriate patient population as well as endpoints for evaluation in a Phase 3 study. The majority of patients enrolled presented with musculoskeletal disease compared to a limited number who presented with liver and cardiac symptoms. Patients spanned a wide age range from ten months to 58 years old. Prior to initiating treatment with UX007, 27 of the 29 patients were on the standard of care MCT oil therapy. Following discontinuation of MCT oil therapy, the average dose of UX007 through 24 weeks was 30% of total daily caloric intake.

Improvements were observed in both measures of exercise tolerance (cycle ergometry and 12 minute walk test) in musculoskeletal patients who performed the tests. The three areas of evaluation with cycle ergometry included workload (measured in watts produced at a fixed heart rate), respiratory exchange ratio, or RER, a measure of energy supply, and duration of cycling. Patients showed improvements in both workload and duration and no change in RER. At week 24, seven patients (who qualified by age and performed the test at baseline) produced a mean 60% increase in watts over baseline representing a mean increase of +446.8 watts (median: +127.5; min, max: -388, +2438). The mean duration was increased in 3 patients who did not complete all 40 minutes at baseline. Eight qualified patients demonstrated a mean 28% increase of +188 meters (median: 93.5; min, max: -80, +880) at week 18 in the 12-minute walk test. These patients also experienced an improvement in the mean energy expenditure index (a ratio of heart rate per meter walked). The data on the 12 minute walk test and cycle ergometry together support an improvement in muscle function and exercise efficiency in a small number of patients that would need to be confirmed in larger controlled studies. Patients with liver/hypoglycemia and cardiac disease were limited, 3 and 2 respectively, but they qualified for entry due to frequent history of events and will contribute to the event rate measurement over 78 weeks.

Overall major medical events appeared to decrease in the 25 patients who completed the 24 weeks of treatment when compared to the reported event rate in these patients approximately 18 months prior to treatment with UX007. These data are preliminary and require significantly more time for proper evaluation at the 78 week time-point. The major medical event rate aggregates events related to hypoglycemia, rhabdomyolysis, and cardiomyopathy.

Improvements in patient-reported quality of life scores (SF-12) were observed in adult patients, but no difference was seen in parent-reported scores (SF-10) for pediatric patients. The Peabody Developmental Motor Score (PDMS-2) and the Pediatric Disability Inventory (PEDI-CAT), also showed no impairment in the overall patient population at baseline and no change after 24 weeks.

Four of the 29 enrolled patients discontinued prior to 24 weeks. One patient discontinued due to diarrhea in week 1, which resolved within a few days of discontinuation, and three patients withdrew consent (weeks 1, 8, 8) for reasons not attributed to treatment with UX007. All other patients opted to continue treatment in the extension phase of the study. There have been no deaths. One serious related adverse event of moderate gastroenteritis with vomiting was considered treatment-related. A viral infection was

suspected, but the investigator could not rule out cause by UX007 given the proximity to dosing. That patient continues to be treated in the study and maintained dosing throughout the event, which has now resolved. Overall, 18 patients (62%) had treatment-related adverse events, most of which were mild-to-moderate in nature. The most common treatment-related adverse events were diarrhea, abdominal/gastrointestinal pain, and vomiting. Some gastrointestinal events were managed by adjusting dosing or dosing with food. The most common adverse events, including those not deemed treatment-related, were viral infections, gastrointestinal disorders, rhabdomyolysis, fever, and headache.

We are planning to initiate a Phase 3 study in LC-FAOD patients in 2017 based on these interim Phase 2 data. We intend to provide further details after completing discussions with the regulatory authorities.

#### ***UX007 for the treatment of Glut1 DS***

We are also developing UX007 for patients with glucose transporter type-1 deficiency syndrome, or Glut1 DS. Glut1 DS is caused by a mutation affecting the gene that codes for Glut1, which is 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 effectiveness of the diet in the treatment of developmental delay and movement disorders has not been confirmed. 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.

UX007 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 UX007.

In March 2014, we initiated a Phase 2 global, randomized, double-blind, placebo-controlled, parallel-group clinical study that plans to 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 6-week baseline period and subsequent 8-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 UX007 through week 52. In order to accelerate enrollment, we amended the enrollment criteria to also include patients with only absence seizures. The study will enroll up to 40 patients with data expected in the second half of 2016, subject to enrollment.

In April 2015, positive data from an investigator-sponsored study of UX007 for the treatment of movement disorders associated with Glut1 DS were presented at the American Academy of Neurology Annual Meeting. The data showed a statistically significant 90% reduction in movement disorder events after treatment with UX007 ( $p=0.028$ ) and a statistically significant increase in events after withdrawal from treatment with UX007 ( $p=0.043$ ). Based on these study results, and following an End-of-Phase 2 meeting with the FDA, in November 2015 we announced an update to our development plan for UX007 in Glut1 DS patients. We now plan to initiate a Phase 3 study in Glut1 DS patients with the movement disorder phenotype in the second half of 2016. The study is intended to be a randomized, double-blind, placebo-controlled, double cross-over study. The primary endpoint will be an assessment of the impact of UX007 on movement disorder events as recorded by a patient diary that will be further refined in discussions with the FDA. If the data are positive, the two studies are intended to support a new drug application, or NDA, filing for the treatment of Glut1 DS.

#### ***Ace-ER (UX001) for the treatment of GNE myopathy***

We are developing aceneuramic acid extended-release (Ace-ER), formerly known as sialic acid extended-release (SA-ER), which is an extended-release, oral formulation of sialic acid for the treatment of GNE myopathy, which is also known as hereditary inclusion body myopathy, or HIBM. GNE myopathy 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 GNE myopathy 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, GNE myopathy patients have a sialic acid deficiency, which interferes with muscle function, leading to myopathy and atrophy. Patients typically lose major muscle function within ten to 20 years of diagnosis. There is no approved drug therapy for GNE myopathy.

Ace-ER is intended as a potential substrate replacement therapy designed to address sialic acid deficiency and restore muscle function in GNE myopathy patients. We have conducted a Phase 2 randomized, double-blind, placebo-controlled study of Ace-ER in 47 GNE myopathy 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 Ace-ER per day. After 24 weeks, placebo patients crossed over to either three grams or six grams total daily dose, 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 Ace-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. Ace-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 the most commonly reported adverse events were gastrointestinal in nature and pain related to muscle biopsy procedures.

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 six 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 Ace-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-gram data did not suggest any clinically meaningful advantage over six grams, the 12-gram data do provide additional data that supported clinical activity with Ace-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. Throughout the approximately two-year study period, treatment with Ace-ER appeared to slow the progression of upper extremity disease when compared to the 24-week placebo group extrapolated out to two years.

We initiated a randomized, double-blind, placebo-controlled 48-week pivotal Phase 3 study of Ace-ER in approximately 80 patients with GNE myopathy in May 2015. The FDA agreed with the 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. Data from the Phase 3 study are expected in 2017.

In October 2015 we announced the filing and acceptance of a Marketing Authorization Application, or MAA, seeking conditional approval from the EMA based on our Phase 2 study results for the use of six grams per day of Ace-ER tablets in the treatment of GNE myopathy. The CHMP opinion on the conditional marketing authorization is expected in the second half of 2016.

## **Preclinical Pipeline**

### ***rhPPCA (UX004) for the treatment of galactosialidosis***

Recombinant human protective protein cathepsin-A, or rhPPCA, which we 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 no currently 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 with plans to file an investigational new drug application, or IND, in 2017.

### ***Collaboration with Arcturus Therapeutics, Inc. for mRNA therapeutics***

We signed a research collaboration and license agreement with Arcturus Therapeutics, Inc. to develop mRNA therapeutics for select rare disease targets in October 2015. The Arcturus collaboration may help us address a wider range of rare diseases than possible with current approaches. As part of the collaboration, Arcturus will utilize its UNA Oligomer™ chemistry and LUNAR™ nanoparticle delivery platform to initially design and optimize mRNA therapeutics for two targets selected by us; we also have the option to add up to eight additional targets during the collaborative research period.

### ***Other preclinical programs***

We continue to work on other compounds in various preclinical stages of development.

## **Competition**

The commercialization of new drugs is competitive, and we may face worldwide competition from individual investigators, major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, nutraceutical companies, and ultimately biosimilar and generic companies. Our competitors may develop or market therapies that are more effective, safer, or less costly than any that may be commercialized by us, or may obtain regulatory approval for their therapies more rapidly than we may obtain approval for ours.

The acquisition or licensing of pharmaceutical products is also very competitive, and a number of more established companies, which have acknowledged strategies to license or acquire products, may have competitive advantages as may other emerging companies taking similar or different approaches to product acquisitions. These established companies may have a competitive advantage over us due to their size, cash flows, and institutional experience.

With respect to KRN23, although we are not aware of any other products currently in clinical development for the treatment of XLH, it is possible that competitors may produce, develop, and commercialize therapeutics, or utilize other approaches such as gene therapy, to treat XLH. Most pediatric patients with XLH are managed using oral phosphate replacement and/or vitamin D therapy, which is relatively inexpensive and therefore may adversely affect our ability to commercialize KRN23, if approved, in some countries.

With respect to rhGUS and rhPPCA, we are not aware of any other compounds currently in clinical development for MPS 7 or galactosialidosis, but it is possible that other companies may produce, develop, and commercialize compounds that might treat these diseases. Additionally, gene therapy and other therapeutic approaches may emerge for the treatment of lysosomal diseases. Bone marrow or stem cell transplants have also been used in MPS 7 and in other lysosomal storage diseases and represent a potential competing therapy. Stem cell transplants have been effective in treating soft tissue storage and in having an impact on brain disease, but have not to date proven effective in treating bone and connective tissue disease. Typically, enzyme replacement therapy has had an impact on bone and connective tissue disease in other disorders when patients were treated early.

With respect to UX007/triheptanoin, there are currently no approved drugs or treatments for patients with LC-FAOD or Glut1 DS. LC-FAOD is commonly treated with diet therapy and MCT oil, and UX007 would compete with MCT oil. Glut1 DS is commonly treated with ketogenic diet and antiepileptic drugs. UX007 may compete with these approaches, though it may potentially be used in combination. Although we believe that UX007 should be considered a drug and will be regulated that way, it is possible that other companies or individuals may attempt to produce triheptanoin for use in LC-FAOD, Glut1 DS, and other patients by attempting to sell the product via a nutritional supplement or medical food pathway. Investigators are testing triheptanoin in clinical studies across multiple indications, including LC-FAOD and Glut1 DS. For example, B. Braun Medical Inc., or B. Braun, has applied for and received orphan drug designation for triheptanoin for the treatment of certain types of LC-FAOD in Europe; however, we are not aware of any ongoing clinical development activities by B. Braun. It is also possible that other companies may produce, develop, and commercialize other medium odd-chain fatty acids, or completely different compounds, to treat LC-FAOD and Glut1 DS. Other companies may also utilize other approaches, such as gene therapy, to treat LC-FAOD and Glut1 DS.

With respect to Ace-ER, although there are currently no approved drug therapies for the treatment of HIBM, it is possible that others may develop alternative approaches to the treatment of HIBM, including other metabolites from the sialic acid pathway, prodrugs, other drug therapies, and gene therapy. We are aware of a program at the National Institutes of Health that is investigating the use of another metabolite in the sialic acid pathway, N-acetyl mannosamine, or ManNAc, for the treatment of HIBM. Escala Therapeutics Inc. (a subsidiary of Fortress Biotech) acquired from New Zealand Pharmaceuticals Ltd, a license from the NIH for the development of ManNAc for the treatment of GNE Myopathy. New Zealand Pharmaceuticals manufactures ManNAc and is its exclusive global supplier to Escala Therapeutics. A Phase 1 clinical study has been completed and an open-label, three-month Phase 2 study is ongoing.

Many of our competitors have substantially greater financial, technical, and human resources than we have. Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that addresses unmet medical needs and creates value in patient therapy.

## **License Agreements**

### ***Kyowa Hakko Kirin***

In August 2013, we entered into a collaboration and license agreement with Kyowa Hakko Kirin Co., Ltd. (KHK), which was amended in August 2015. Under the terms of this collaboration and license agreement, we and KHK will collaborate on the development and commercialization of certain products containing KRN23, an antibody directed towards FGF23, in the field of orphan diseases in the United States and Canada, or the “profit-share territory”, and in the European Union, Switzerland, and Turkey, or the European territory, and we will have the right to develop and commercialize such products in the field of orphan diseases in Mexico and Central and South America, or Latin America. In the field of orphan diseases, and except for ongoing studies being conducted by KHK, we will be the lead party for development activities in the profit-share territory and in the European territory until the applicable transition date; we will also be the lead party for core development activities conducted in Japan and Korea, provided that the core development plan related to Japan and Korea shall be limited to clinical trials mutually agreed to by the Company and KHK. We will share the costs for development activities in the profit share territory and European territory conducted pursuant to the development plan before the applicable transition date equally with KHK and KHK shall be responsible for 100% of the costs for development activities in Japan and Korea. On the applicable transition date in the profit-share territory and the European territory, KHK will become the lead party and be responsible for the costs of the development activities. However, we will continue to share the costs of the studies commenced prior to the applicable transition date equally with KHK. We have the primary responsibility for

conducting certain research and development activities. We are obligated to provide assistance in accordance with the agreed upon development plan as well as participate on various committees. If KRN23 is approved, we and KHK will share commercial responsibilities and profits in the profit share territory until the applicable transition date, KHK will commercialize KRN23 in the European territory, and we will develop and commercialize KRN23 in Latin America. KHK will manufacture and supply KRN23 for clinical use globally and will manufacture and supply KRN23 for commercial use in the profit share territory and Latin America.

In the profit share territory, KHK will book sales of products and we will have the sole right to promote the products for a specified period of time, with KHK increasingly participating in the promotion of the products until five years from commercial launch, after which KHK will have the sole right to promote the products, subject to a limited promotion right retained by us. In the European territory, KHK will book sales of products and have the sole right to promote and sell the products. In Latin America, we will book sales of products and have the sole right to promote and sell the products.

The profit or loss from commercializing products in the profit-share territory, until the applicable transition date, will be shared between us and KHK on a 50/50 basis. Thereafter, we will be entitled to receive a tiered double-digit revenue share in the mid-to-high 20% range in the profit share territory, intended to approximate the profit share. We will also be entitled to receive a royalty of up to 10% on net sales in the European territory. In Latin America, we will pay to KHK a low single-digit royalty on net sales. Our and KHK's obligations to pay royalties will continue on a country-by-country basis for so long as we or KHK, as applicable, are selling products in such country.

KHK will supply all quantities of product for clinical studies. KHK will also supply all quantities of product for commercial sales in the profit-share territory and in Latin America. The supply price to us for commercial sales in the profit-share territory and in Latin America will be determined based on a fixed double-digit percentage of net sales.

The collaboration and license agreement will continue for as long as products in the field of orphan diseases are sold in the profit-share territory, European territory, or Latin America, unless the agreement is terminated in accordance with its terms.

KHK may terminate the agreement in certain countries or territories based upon our failure to meet certain milestones. Specifically, if we do not obtain U.S. or European marketing approval of KRN23 for the treatment of XLH by a certain date, or make a first commercial sale, on a country-by-country basis, in Latin America by certain deadlines, KHK may terminate the agreement only with respect to the applicable territory or country in which the milestone was not timely met. In certain circumstances, we have the right to obtain an extension of the applicable deadline by making a payment to KHK in the low single-digit to low double-digit millions of dollars, depending on the milestone. Also, in the event of the occurrence of certain excusable delays, the deadline for meeting the applicable milestone above is extended to account for the period of the delay. Furthermore, either party may terminate the agreement for the material breach or bankruptcy of the other party. In any event of termination by KHK, unless such termination is the result of KHK's termination for certain types of breach of the agreement by us, we may receive low single-digit to low double-digit royalties on net post-termination sales by KHK in one or more countries or territories, the amount of which varies depending on the timing of, and reason for, such termination. In any event of termination, our rights to KRN23 under the agreement and our obligations to share development costs will cease, and the program will revert to KHK, worldwide if the agreement is terminated as a whole or solely in the terminated countries if the agreement is terminated solely with respect to certain countries.

#### ***Saint Louis University***

In November 2010, we entered into a license agreement with Saint Louis University, or SLU, wherein SLU granted us certain exclusive rights to intellectual property related to GUS. Under the terms of the license agreement, SLU granted us an exclusive worldwide license to make, have made, use, import, offer for sale, and sell therapeutics related to SLU's beta-glucuronidase product, such as our rhGUS product candidate, for use in the treatment of human diseases. Under this agreement, we agreed to use best efforts to develop and commercialize a licensed product as soon as practicable consistent with sound and reasonable business practices and judgment.

Under the license agreement, we paid SLU a nominal up-front fee, which was recorded as a research and development expense. We will make a milestone payment of \$0.1 million upon approval of a glucuronidase-based enzyme therapy for treatment of MPS 7. Additionally, upon reaching a certain level of cumulative worldwide sales of the product, we will pay to SLU a low single-digit royalty on net sales of the licensed products in any country or region, subject to certain potential deductions. Our obligation to pay royalties to SLU continues on a country-by-country basis until the expiration of the last-to-expire licensed patent covering the product in such country or, in the United States, Japan, and the EU, until the later expiration of any orphan drug exclusivity. We may deduct a portion of the royalty owed if a third-party license is required. We may terminate the agreement for convenience at any time and SLU may terminate the agreement for our material breach, bankruptcy, or challenge of the licensed patents or technology, and SLU may terminate the agreement or render our license non-exclusive if we fail to meet our diligence obligations. Unless terminated as set forth above, this license agreement continues in full force and effect until the latest of expiration of the last patent based on technology licensed under the agreement, at which point our license becomes fully paid.

### ***Baylor Research Institute***

In September 2012, we entered into a license agreement with Baylor Research Institute, or BRI, whereby we exclusively licensed certain intellectual property related to triheptanoin for North America and paid BRI an up-front fee of \$0.3 million. The license includes patents, patent applications, know-how, and intellectual property related to the composition and formulation of triheptanoin as well as its use in treating a number of orphan diseases, including FAOD. The license grant includes the sole right to develop, manufacture, and commercialize licensed products for all human and animal uses. In June 2013, we exercised our option to license this intellectual property outside of North America and paid BRI the \$0.8 million fee associated with this option exercise. Under the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize licensed products in select orphan indications. If we fail to meet our diligence obligations with respect to a specified orphan indication or set of orphan indications, BRI may convert our license to a non-exclusive license with respect to such orphan indication or set of orphan indications until we receive regulatory approval for licensed products in the applicable orphan indication or set of orphan indications. We are also obligated to pay a mid-single digit royalty on net sales to BRI, subject to certain reductions and offsets. Our obligation to pay royalties to BRI continues on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the first regulatory exclusivity granted with respect to such product in such country or the expiration of the last-to-expire licensed patent claiming such product in such country, in each case in connection with approval in such country for FAOD or an orphan disease covered by our license from BRI. We may make future payments of up to \$10.5 million contingent upon attainment of certain development milestones and \$7.5 million if certain sales milestones are achieved. We may terminate the agreement for convenience at any time and either we or BRI may terminate the agreement for the material breach or bankruptcy of the other party. If we terminate for BRI's breach or bankruptcy, our license from BRI will remain in effect, subject to our continued payment of reduced milestones and royalties. Unless terminated for convenience or material breach or bankruptcy, as applicable, this license agreement continues in full force and effect, on a product-by-product and country-by-country basis, until our royalty obligations expire, at which point our license from BRI with respect to such product in such country becomes irrevocable, perpetual, fully paid and royalty-free.

### ***Nobelpharma***

In September 2010, we entered into a collaboration and license agreement with Nobelpharma Co., Ltd. (Nobelpharma), which was amended in August 2015. Under the terms of this collaboration and license agreement, each party granted the other party a worldwide exclusive license under certain of that party's intellectual property related to the compound identified as N-acetylneuraminic acid, also known as sialic acid, to develop, manufacture, and commercialize products. Nobelpharma's licensed territory includes Japan and certain other Asian countries, and our licensed territory includes the rest of the world. The parties conduct development independently, and each party is obligated to make commercially reasonable efforts to file an investigational new drug application, or IND, for licensed products in its territory and, in our case, to obtain patent term extensions and data exclusivity in Europe and North America, and share with the other party all data, documentation, and information that is generated in conducting such activities. Nobelpharma must use commercially reasonable efforts to supply us with the sialic acid drug substance. Either Nobelpharma or we can terminate this supply arrangement for convenience, at which point Nobelpharma would provide technical assistance to allow us to manufacture the sialic acid drug substance ourselves. If we choose to manufacture the sialic acid drug substance, Nobelpharma will have the right to purchase the sialic acid drug substance from us and we will use commercially reasonable efforts to supply Nobelpharma with the sialic acid drug substance.

Under the collaboration and license agreement, we paid Nobelpharma an upfront fee of \$0.1 million (10 million Yen), which was recorded as research and development expense in 2010, and also issued 76,567 shares of common stock to Nobelpharma. In addition, we are required to make certain payments to Nobelpharma based upon achievement of certain development and approval milestones. We have paid \$0.5 million in development milestone payments since the inception of the agreement through December 31, 2015. The remaining total aggregate payments, if all milestones are achieved by Nobelpharma, would be 200 million Yen (approximately \$1.7 million based on the exchange rate at December 31, 2015). We will pay a mid-single digit royalty on net sales in our territory and will receive a mid-single digit royalty on net sales in the Nobelpharma territory, excluding Japan, if such product sales are ever achieved. Net sales, as defined in the collaboration and license agreement, represent the net sales of products whereby the licensed compound is the active ingredient. If the products include other active ingredients, the portion of the net sales allocated to the licensed compound would be used in determining the royalty payments.

If either party terminates the agreement, the terminating party's license will become irrevocable and royalty-free. Unless terminated for material breach or bankruptcy, as applicable, this license agreement continues in full force and effect, on a country-by-country basis, until the date of the first launch of a generic product of the licensed product in a country.

## **AAIPharma**

In March 2011, we entered into a license agreement with AAIPharma Services Corp., or AAIPharma. Under the terms of this license agreement, AAIPharma granted us a fully paid-up, royalty-free, exclusive, perpetual, and irrevocable license to research, develop, make, have made, use, import, offer for sale, and sell products incorporating AAIPharma's controlled release matrix solid dose oral tablet technology for use in connection with sialic acid for the treatment of HIBM or distal myopathy with rimmed vacuoles. Under the license agreement, we will pay a mid-single digit percentage of any sublicense revenue received by us related to the sublicense of AAIPharma technology. As consideration, we agreed to provide preclinical and clinical data to AAIPharma. AAIPharma is responsible for patent prosecution and maintenance, subject to our right to review and comment on such prosecution and maintenance. We may terminate the agreement for convenience at any time and either party may terminate the agreement for the material breach or bankruptcy of the other party.

## **HIBM Research Group**

In April 2012, we entered into an exclusive license agreement with HIBM Research Group, or HRG, wherein HRG granted us an exclusive, worldwide license to certain intellectual property related to the treatment of HIBM and related conditions using substrate replacement therapy.

Under the terms of the license agreement, we paid HRG a nominal up-front fee, which was recorded as a research and development expense. We will make future payments contingent upon attainment of various development and approval milestones of up to \$0.3 million in the aggregate. Additionally, we will pay to HRG a royalty of less than 1% of net sales of products, if any. Our obligation to pay royalties to HRG continues on a product-by-product and country-by-country basis until the expiration of the last-to-expire licensed patent claiming such product in such country, or the later expiration of orphan drug exclusivity in certain countries. We are obligated to make commercially reasonable efforts to develop and commercialize a substrate replacement therapy for HIBM. We may terminate the agreement for convenience at any time and either party may terminate the agreement for the material breach or bankruptcy of the other party. We must also terminate the agreement if we terminate our HIBM substrate replacement therapy program. Unless terminated for convenience, for our termination of our HIBM substrate replacement therapy program, or for material breach or bankruptcy, as applicable, this license agreement continues in full force and effect, on a product-by-product and country-by-country basis, until the expiration date of the last-to-expire licensed patent claiming such product in such country, or the later expiration of orphan drug exclusivity in certain countries, at which point our license becomes irrevocable, perpetual, fully paid, and royalty-free.

## **St. Jude Children's Research Hospital**

In September 2012, we entered into a license agreement with St. Jude Children's Research Hospital, or St. Jude, wherein St. Jude granted us certain exclusive rights to intellectual property related to rhPPCA. Under the terms of the license agreement, St. Jude granted us an exclusive license under certain know-how to research, develop, make, use, offer to sell, import, and otherwise commercialize and exploit certain PPCA protein products to treat, prevent, and/or diagnose galactosialidosis and other monogenetic diseases. We agreed to make commercially reasonable efforts to develop and commercialize at least one licensed product.

Under the license agreement, we paid St. Jude a nominal up-front fee, which was recorded as research and development expense. Additionally, we will pay to St. Jude a royalty of less than 1% on net sales of these products for so long as such products retain orphan drug exclusivity, on a country-by-country basis. We may terminate the agreement for convenience at any time and St. Jude may terminate the agreement for our material breach of the agreement. Unless terminated for convenience or material breach, as applicable, this license agreement continues in full force and effect, until our royalty obligations expire, at which point our license becomes irrevocable, perpetual, fully paid, and royalty-free.

## **Patents and Proprietary Rights**

The proprietary nature of, and protection for, our product candidates, processes, and know-how are important to our business. Our success depends in part on our ability to protect the proprietary nature of our product candidates, technology, and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. We seek patent protection in the United States and internationally for our product candidates and other technology. Our policy is to patent or in-license the technology, inventions and improvements that we consider important to the development of our business. In addition to patent protection, we intend to use other means to protect our proprietary rights, including pursuing marketing or data exclusivity periods, orphan drug status, and similar rights that are available under regulatory provisions in certain countries, including the United States, Europe, Japan, and China. See "U.S. Government Regulation — Orphan Designation and Exclusivity," "U.S. Government Regulation — Pediatric Studies and Exclusivity," "U.S. Government Regulation — Patent Term Restoration," "U.S. Government Regulation — Biosimilars and Exclusivity," "U.S. Government Regulation — Abbreviated New Drug Applications for Generic Drugs," "U.S. Government Regulation — Hatch-Waxman Patent Certification and the 30-Month Stay," and "European Union/Rest of World Government Regulation — Orphan Designation and Exclusivity" below for additional information.

We also rely on trade secrets, know-how, and continuing innovation to develop and maintain our competitive position. We cannot be certain that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology.

We seek regulatory approval for our products in disease areas with high unmet medical need, significant market potential, and where we expect to have a proprietary position through patents covering various aspects of our products, such as composition, dosage, formulation, use, and manufacturing process, among others. Our success depends in part on an intellectual property portfolio that supports our future revenue streams and erects barriers to our competitors. We are maintaining and building our patent portfolio through filing new patent applications, prosecuting existing applications, and licensing and acquiring new patents and patent applications.

Despite these measures, any of our intellectual property and proprietary rights could be challenged, invalidated, circumvented, infringed or misappropriated, or such intellectual property and proprietary rights may not be sufficient to achieve or maintain market exclusivity or otherwise to provide competitive advantages. For more information, please see “Risks Related to Our Intellectual Property.”

As of February 19, 2016, we own 3 issued U.S. patent and 9 pending U.S. patent applications as well as corresponding patents and patent applications internationally. In addition, as of February 19, 2016, we have licensed 15 issued U.S. patents and 35 pending U.S. patent applications, as well as corresponding foreign patents and applications from third parties, on an exclusive basis. With respect to our issued patents in the United States and Europe, we are also entitled to obtain a patent term extension to extend the patent expiration date. For example, in the United States, we can apply for a patent term extension of up to five years for one of the patents covering a product once the product is approved by the FDA. The exact duration of the extension depends on the time we spend in clinical studies as well as getting marketing approval from the FDA. The patent portfolios for our five leading product candidates as of February 19, 2016 are summarized below.

#### *KRN23*

We have rights from KHK to patents and patent applications relating to KRN23, a fully human monoclonal antibody against FGF23, and its use for the treatment of XLH and various other hypophosphatemic conditions. Pursuant to this license, we share rights to 20 issued patents, including 3 U.S. patents and 2 pending U.S. applications, as well as patents and applications in other jurisdictions covering generic and specific antibodies against FGF23 as well as their use for the treatment of XLH and related conditions. The patent terms for issued patents in the United States are from 2022 to 2029 (without patent term extension). The projected patent terms for pending applications in the United States are from 2028 to 2035. We intend to pursue marketing and orphan drug exclusivity periods that are available to us under regulatory provisions in certain countries. KRN23 has received orphan drug designation in the United States and Europe for the treatment of XLH.

#### *rhGUS*

We have no issued patents covering rhGUS but we have 2 pending U.S. patent applications and a corresponding international patent application directed to compositions with certain characteristics that are useful for the enzyme replacement therapy for the treatment of multi-system lysosomal storage disease. Throughout clinical research and development, we also intend to file patent applications directed to various aspects of the treatment therapy including dosage, regimen, formulation, and manufacturing, among others. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries. rhGUS has received orphan drug designation in both the United States and Europe for the treatment of MPS 7.

#### *UX007*

We are the licensee or owner of patents and patent applications relating to UX007 and its use for a number of diseases including FAOD and Glut1 DS. In particular, we have an exclusive license from Baylor Research Institute, or BRI, with respect to its UX007 patent portfolio. We have licensed from BRI 27 issued patents, including 9 U.S. patents and 5 pending U.S. applications and patents and applications in other jurisdictions covering composition, formulation, use and manufacturing of UX007 and related odd carbon fatty acids. The patent terms for issued patents in the United States are from 2020 to 2025 (without patent term extension). The projected patent terms for pending applications in the United States are from 2020 to 2033. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries. UX007 for the treatment of FAOD and Glut1 DS has received orphan drug designation in the United States.

### *Ace-ER*

We are the licensee or owner of patents and patent applications relating to sialic acid and its use for the treatment of HIBM. We own or have rights to 2 issued U.S. patents and 6 pending U.S. applications and patents and applications in other jurisdictions covering the use of sialic acid for the treatment of HIBM, as well as extended release formulations of sialic acid. The patent terms for the issued patents in the United States are from 2031 to 2032 (without patent term extension). The projected patent terms for pending applications in the United States are from 2028 to 2031.

We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries. Ace-ER has received orphan drug designation in both the United States and the EU for the treatment of HIBM.

### *rhPPCA*

We are the licensee of patent applications relating to the use of rhPPCA for the treatment of neurodegenerative diseases. Specifically, we have an exclusive license from the St. Jude Children's Research Hospital, or St. Jude. Furthermore, we intend to build a patent portfolio directed to rhPPCA compositions with certain characteristics that are useful for the enzyme replacement therapy for the treatment of autosomal recessive lysosomal storage disease as well as various aspects of the treatment therapy including dosage, regimen, formulation, manufacturing, etc. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries.

### **Trademarks**

We have filed trademark applications for the Ultragenyx brand in the U.S. and multiple other jurisdictions.

### **Other**

We rely upon unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We seek to protect our ownership of know-how and trade secrets through an active program of legal mechanisms including assignments, confidentiality agreements, material transfer agreements, research collaborations, and licenses.

### **Manufacturing**

We currently contract with third parties for the manufacturing and testing of our product candidates for preclinical studies and clinical studies and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of contracted manufacturing and reliance on collaboration partners is relatively cost-efficient and has eliminated the need for our direct investment in manufacturing facilities and additional staff early in development. Although we rely on contract manufacturers, we have personnel with extensive manufacturing experience to oversee our contract manufacturers.

To date, our third-party manufacturers have met our manufacturing requirements. We expect third-party manufacturers to be capable of providing sufficient quantities of our product candidates to meet anticipated full scale commercial demands. To meet our projected needs for commercial manufacturing, third parties with whom we currently work might need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

### *KRN23*

The drug substance and drug product for KRN23 are made by KHK in Japan under the collaboration and license agreement with KHK. The cell line to produce KRN23 is specific for this product and is in KHK's control. All other raw materials are commercially available.

### *rhGUS*

rhGUS drug substance and drug product are manufactured by Rentschler Biotechnologie GmbH, or Rentschler, under a development and clinical supply agreement executed in August 2012. Pursuant to the clinical supply agreement, we have agreed not to source larger quantities of drug substance or drug product from another supplier than from Rentschler in any given year. The supply agreement will continue in full force and effect until all clinical services have been completed or terminated per the terms of the supply agreement. Either party may terminate the supply agreement if the other party fails to pay any sum payable under the supply agreement within 30 days after a written demand is issued after the original due date, if the other party makes a material misrepresentation or commits a material breach of its obligations under the supply agreement and fails to cure such breach within specified time periods if curable, if the other party ceases to carry on its business for a period no less than 60 days, or if a party experiences certain insolvency events. Additionally, either party may terminate the supply agreement upon 30 days' prior written notice if the Steering Committee concludes that the services required under the supply agreement cannot be performed and we may terminate the agreement at any time before completion of the services rendered pursuant to the agreement upon 60 days' prior written notice. The cell line to produce rhGUS is specific for this product and is in our control and stored in multiple secure locations. All other raw materials are commercially available.

### *UX007*

The pharmaceutical-grade drug substance for UX007 is manufactured by Cremer Oleo GmbH & Co. KG in Germany under an exclusive worldwide supply agreement, subject to certain limitations, executed in 2012. The supply agreement has an initial term of three years; thereafter, the agreement shall be automatically renewed for additional two-year periods unless either party notifies the other party of its intention not to renew in writing at least three calendar months before the expiration of the then current term. Additionally, if a party materially breaches an obligation under the agreement and does not cure such breach within 60 days of receiving notice of the breach from the non-breaching party, the non-breaching party may terminate the agreement immediately upon written notice to the breaching party. UX007 drug product manufacturing has been done with more than one party and is not considered a very specialized task.

### *Ace-ER*

The drug substance for Ace-ER is currently manufactured by Sanyo Fine Co., Ltd. in Japan through the license agreement with Nobelpharma. The Ace-ER drug product is manufactured by AAIPharma under our license agreement and accompanying purchase orders with AAIPharma. We are in the process of securing secondary sources of drug substance and drug product for SA-ER. Manufacture of the drug substance requires a specialized enzyme-catalyzed step, and a secondary source of the enzyme itself is also under development. All raw materials to produce the drug substance and drug product are commercially available. The cell line to produce the specialized enzyme is under our control and is stored in multiple secured locations.

### *rhPPCA*

No commercial supplier has yet been selected to manufacture rhPPCA. The cell line to produce rhPPCA is specific for this product and is in our control and stored in multiple secure locations. All other raw materials are commercially available. We are currently developing a manufacturing process for rhPPCA.

## **Sales and Marketing**

We are building capabilities in the United States, Europe and Latin America necessary to effectively support the commercialization of our product candidates. The commercial infrastructure for rare disease products typically consists of a targeted, specialty field organization that calls on a limited and focused group of physicians supported by field management, medical liaisons, internal support, and distribution support. One challenge unique to commercializing therapies for rare diseases is the difficulty in identifying eligible patients due to the very small and sometimes heterogeneous disease populations. Our management team is experienced in maximizing patient identification for both clinical development and commercialization purposes in rare diseases.

Additional capabilities important to the rare disease marketplace include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, and government accounts. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any of our product candidates will be approved.

Outside of the United States and Europe, where appropriate, we may elect in the future to utilize strategic partners, distributors, or contract organizations to assist in the commercialization of our products. In certain instances, such as in Latin America, we may consider building our own commercial infrastructure.

## Government Regulation

Government authorities in the United States (including federal, state, and local authorities) and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, pricing, and export and import of pharmaceutical products, such as those we are developing. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

### U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biologics under the FDCA and the Public Health Service Act, or PHSA, and its implementing regulations. FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. Drugs and biologics are also subject to other federal, state, and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the drug development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests and preclinical animal studies performed in accordance with the Good Laboratory Practices, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical studies may begin and must be updated annually;
- approval by an independent institutional review board, or IRB, or ethics committee representing each clinical site before each clinical study may be initiated;
- performance of adequate and well-controlled human clinical studies to establish the safety and efficacy of the product candidate for each proposed indication;
- preparation of and submission to the FDA of an NDA, or biologics license application, or BLA, after completion of all pivotal clinical studies;
- potential review of the product application by an FDA advisory committee, where appropriate and if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the proposed drug substance and drug product are produced to assess compliance with Good Manufacturing Practices, or GMP;
- FDA will typically inspect one or more clinical sites to assure compliance with Good Clinical Practices, or GCP; and
- FDA review and approval of an NDA or BLA prior to any commercial marketing or sale of the drug in the United States.

The preclinical and clinical testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Additionally, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical studies can begin.

### Clinical Studies

Clinical studies involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with protocols and GCP. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical study site's IRB, before the studies may be initiated, and the IRB must monitor the study until completed. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

The clinical investigation of a drug is generally divided into three or four phases. Although the phases are usually conducted sequentially, they may overlap or be combined.

- *Phase 1.* The drug is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, pharmacokinetics and pharmacologic actions of the investigational new drug in humans, and if possible, to gain early evidence on effectiveness.
- *Phase 2.* The drug is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy.

- *Phase 3.* The drug is administered to an expanded patient population, generally at geographically dispersed clinical study sites to generate enough data to statistically evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational new drug product, and to provide an adequate basis for product approval.
- *Phase 4.* In some cases, additional studies and patient follow-up are conducted to gain experience from the treatment of patients in the intended therapeutic indication. The FDA may condition approval of an NDA or BLA for a product candidate on the sponsor's agreement to conduct additional clinical studies after approval. In other cases, a sponsor may voluntarily conduct additional clinical studies after approval to gain more information about the drug. Such post-approval studies are typically referred to as Phase 4 clinical studies. Failure to timely conduct required Phase 4 clinical trials and follow-up could result in withdrawal of approval for products approved under accelerated approval regulations.

A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can be used to justify the approval of the product. Generally, pivotal studies are Phase 3 studies, but the FDA may accept results from Phase 2 studies if the study design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need and the results are sufficiently robust.

The FDA, the IRB, or the clinical study sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk.

Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee. This group provides recommendations for whether or not a study may move forward at designated check points based on access to certain data from the study. The sponsor may also suspend or terminate a clinical study based on evolving business objectives and/or competitive climate.

The clinical study process can take three to ten years or more to complete, and there can be no assurance that the data collected will support FDA approval or licensure of the product.

#### *Submission of an NDA or BLA to the FDA*

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational new drug product information is submitted to the FDA in the form of an NDA or BLA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs and BLAs is subject to an application user fee. For fiscal year 2016, the application user fee exceeds \$2.3 million, and the sponsor of an approved NDA or BLA is also subject to annual product and establishment user fees, set at \$114,450 per product and \$585,200 per establishment, as well as new application fees in excess of \$1.1 million for supplemental applications with clinical data. These fees are typically increased annually. Applications for orphan drug products are exempted from the NDA and BLA user fees and may be exempted from product and establishment user fees, unless the application includes an indication for other than a rare disease or condition.

An NDA or BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational new drug product to the satisfaction of the FDA.

Once an NDA or BLA has been submitted, the FDA's goal is to review the application within ten months after it accepts the application for filing, or, if the application relates to an unmet medical need in the treatment of a serious or life-threatening condition, six months after the FDA accepts the application for filing. The review process can be significantly extended by FDA requests for additional information or clarification.

## *The FDA's Decision on an NDA or BLA*

The FDA may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA or BLA approval, the FDA may impose additional requirements, such as post-marketing studies and/or a risk evaluation and mitigation strategy (REMS) to help ensure that the benefits of the drug outweigh the potential risks. A REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use. These requirements can materially affect the potential market and profitability of a product. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical study(ies), and/or other significant, expensive and time-consuming requirements related to clinical studies, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. The FDA could also approve the NDA or BLA with a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical studies. Such post-market testing may include Phase 4 clinical studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

## *Expedited Review and Accelerated Approval Programs*

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of NDAs and BLAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition and data demonstrate its potential to address unmet medical needs for the disease or condition. The key benefits of fast track designation are the eligibility for priority review, rolling review (submission of portions of an application before the complete marketing application is submitted), and accelerated approval, if relevant criteria are met. The FDA may grant the NDA or BLA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

The FDA may approve an NDA or BLA under the accelerated approval program if the drug treats a serious condition, provides a meaningful advantage over available therapies, and demonstrates an effect on either (1) a surrogate endpoint that is reasonably likely to predict clinical benefit, or (2) on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit.

In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established the new Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If a drug is designated as breakthrough therapy, FDA will provide more intensive guidance on the drug development program and expedite its review.

## *Post-Approval Requirements*

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to manufacturing, recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with GMP and other requirements. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from GMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with GMP and other aspects of regulatory compliance.

Future FDA and state inspections may identify compliance issues with our pharmacovigilance systems or at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

#### *Orphan Designation and Exclusivity*

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. In addition, the first NDA or BLA applicant to receive orphan drug designation for a particular drug is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years in the United States, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee.

#### *Pediatric Studies and Exclusivity*

NDAs and BLAs must contain data to assess the safety and effectiveness of an investigational new drug product for the claimed indications in all relevant pediatric populations in order to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers if certain criteria are met. Discussions about pediatric development plans can be discussed with the FDA at any time, but usually occur any time between the end-of-Phase II meeting and submission of the NDA or BLA. Unless otherwise required by regulation, the requirements for pediatric data do not apply to any drug for an indication for which orphan designation has been granted.

Pediatric exclusivity is another type of non-patent exclusivity in the United States that may be granted if certain FDA requirements are met, such as FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits, and the applicant agrees to perform and report on FDA-requested studies within a certain time frame. Pediatric exclusivity adds a period of six months of exclusivity to the end of all existing marketing exclusivity and patents held by the sponsor for that active moiety. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application relying on the NDA or BLA sponsor's data.

### *Patent Term Restoration*

Some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA, plus the time between the submission date and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, or USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant NDA or BLA.

### *Biosimilars and Exclusivity*

The Patient Protection and Affordable Care Act of 2010, or Affordable Care Act, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHS Act attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to an FDA-approved reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Complexities associated with the larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being addressed by the FDA. In 2015, the FDA approved the first biosimilar in the U.S., and published a proposed rule and guidance documents relating to various provisions of the BPCI Act. For example, the FDA addressed the naming conventions and labeling of biosimilar products, including whether and how such labeling should include information from reference product labeling and identify a product's approval through the biosimilar pathway. The FDA suggested that shared nonproprietary names may not be appropriate for all biological products, noting that the naming conventions could improve pharmacovigilance, prevent inadvertent substitution among products which have not been determined to be interchangeable, avoid inaccurate perceptions of the safety and effectiveness of biological products based on their licensure pathway, and provide a consistent mechanism for healthcare professionals to identify biological products. The FDA also released guidance recommendations relating to the clinical, scientific, and quality data required to demonstrate biosimilarity.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitting under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) eighteen months after approval if there is no legal challenge, (iii) eighteen months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

### *Abbreviated New Drug Applications for Generic Drugs*

In 1984, with passage of the Hatch-Waxman Act, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, quality and performance characteristics, the strength of the drug, and intended use. A generic drug is "bioequivalent" to the innovator drug if the rate and extent of absorption of the [generic] drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses, or in limited other circumstances.

Upon approval of an ANDA, the FDA indicates that the generic product is “therapeutically equivalent” to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” also referred to as the “Orange Book.” Physicians and pharmacists consider an “AB” therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA’s designation of an “AB” rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if an NDA or supplement includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

#### *Hatch-Waxman Patent Certification and the 30-Month Stay*

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant’s product or a method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product’s listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

#### *European Union/Rest of World Government Regulation*

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. In the EU, for example, a clinical study application, or CTA, must be submitted for each clinical protocol to each country’s national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country’s requirements, the clinical study may proceed.

The requirements and process governing the conduct of clinical studies vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP, the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational medicinal product under EU regulatory systems, we must submit an MAA. The content of the NDA or BLA filed in the United States is similar to that required in the EU, with the exception of, among other things, country-specific document requirements.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product licensing, pricing, and reimbursement vary from country to country.

Countries that are part of the EU, as well as countries outside of the EU, have their own governing bodies, requirements, and processes with respect to the approval of pharmaceutical products. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

#### *Authorization Procedures in the European Union*

Medicines can be authorized in the EU by using either the centralized authorization procedure or national authorization procedures.

- *Centralized procedure.* The EMA implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the European Economic Area, or EEA, which is comprised of the 28 member states of the EU plus Norway, Iceland, and Lichtenstein. This procedure results in a single marketing authorization issued by the EMA that is valid across the EEA. The centralized procedure is compulsory for human medicines that are derived from biotechnology processes, such as genetic engineering; contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions; and officially designated orphan medicines.
- For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.
- *National authorization procedures.* There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:
- *Decentralized procedure.* Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure.* In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

In most cases, a Pediatric Investigation Plan, or PIP, and/or a request for waiver or deferral, is required for submission prior to submitting a marketing authorization application. A PIP describes, among other things, proposed pediatric studies and their timing relative to clinical studies in adults.

#### *New Chemical Entity Exclusivity*

In the EU, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

#### *Orphan Designation and Exclusivity*

In the EU, the EMA's Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU Community and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the medicinal product.

In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

### *Exceptional Circumstances/Conditional Approval*

Orphan drugs or drugs with unmet medical needs may be eligible for EU approval under exceptional circumstances or with conditional approval. Approval under exceptional circumstances is applicable to orphan products and is used when an applicant is unable to provide comprehensive data on the efficacy and safety under normal conditions of use because the indication for which the product is intended is encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, when the present state of scientific knowledge does not allow comprehensive information to be provided, or when it is medically unethical to collect such information. Conditional marketing authorization is applicable to orphan medicinal products, medicinal products for seriously debilitating or life-threatening diseases, or medicinal products to be used in emergency situations in response to recognized public threats. Conditional marketing authorization can be granted on the basis of less complete data than is normally required in order to meet unmet medical needs and in the interest of public health, provided the risk-benefit balance is positive, it is likely that the applicant will be able to provide the comprehensive clinical data, and unmet medical needs will be fulfilled. Conditional marketing authorization is subject to certain specific obligations to be reviewed annually.

### *Accelerated Review*

Under the Centralized Procedure in the EU, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding “clock stops” when additional written or oral information is to be provided by the applicant in response to questions asked by the EMA’s Committee for Medicinal Products for Human Use, or CHMP). The opinion of the CHMP is then transferred to the European Commission, in order to initiate the Decision Making process, which lasts 67 days in total. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days, excluding clock stops.

### ***Pharmaceutical Coverage, Pricing and Reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the approved drugs for a particular indication. Moreover, a payor’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Healthcare Reform Law, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies’ share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on cost containment measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

### **Other Healthcare Laws and Compliance Requirements**

If we obtain regulatory approval for any of our product candidates, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal transparency laws, including the federal Physician Payment Sunshine Act, that requires drug manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The Healthcare Reform Law broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b, effective March 23, 2010. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Healthcare Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

We are also subject to the Foreign Corrupt Practices Act, or FCPA, which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

### **Employees**

As of December 31, 2015, we had 249 full-time employees. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

## **Research and Development**

We recognized \$114.7 million, \$46.0 million, and \$27.8 million in research and development expense in the years ended December 31, 2015, 2014, and 2013, respectively.

## **Product Liability Insurance**

We maintain product liability insurance that provides coverage in the amount of \$10.0 million per incident and \$10.0 million in aggregate.

## **Executive Officers of the Registrant**

Information concerning our executive officers, including their names, ages and certain biographical information can be found in Part III, Item 10. This information is incorporated by reference into Part I of this report.

## **Financial Information about Segments**

We operate in a single accounting segment — the identification, acquisition, development and commercialization of novel products for the treatment of rare and ultra-rare diseases. Refer to Note 1, “Organization and Basis of Presentations” in the Notes to Financial Statements.

## **General Information**

We were incorporated in California in April 2010 and reincorporated in Delaware in June 2011. Our principal executive offices are located at 60 Leveroni Court, Novato, California 94949. Our telephone number is (415) 483-8800 and our e-mail address is [info@ultragenyx.com](mailto:info@ultragenyx.com). Our Internet website address is [www.ultragenyx.com](http://www.ultragenyx.com). No portion of our website is incorporated by reference into this Annual Report on Form 10-K.

You are advised to read this Annual Report on Form 10-K in conjunction with other reports and documents that we file from time to time with the Securities and Exchange Commission, or SEC. In particular, please read our definitive proxy statements, our Quarterly Reports on Form 10-Q and any Current Reports on Form 8-K that we may file from time to time. You may obtain copies of these reports after the date of this annual report directly from us or from the SEC at the SEC’s Public Reference Room at 100 F Street, N.E. Washington, D.C. 20549. In addition, the SEC maintains information for electronic filers (including Ultragenyx) at its website at [www.sec.gov](http://www.sec.gov). The public may obtain information regarding the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. We make our periodic and current reports available on our internet website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

## Item 1A. Risk Factors

*Investing in our common stock involves a high degree of risk. You should carefully consider the following risks, together with all the other information in this report, including our financial statements and notes thereto, before deciding to invest in our common stock. If any of the following risks actually materializes, our operating results, financial condition and liquidity could be materially adversely affected. As a result, the trading price of our common stock could decline and you could lose part or all of your investment.*

### **Risks Related to Our Financial Condition and Capital Requirements**

***We are a clinical-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 a clinical-stage biopharmaceutical company with a limited operating history. We have incurred net losses in each year since our inception in April 2010, including net losses of \$145.6 million, \$59.8 million and \$35.1 million for the years ended December 31, 2015, 2014 and 2013, respectively.

We have devoted substantially all of our financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies, developing manufacturing processes, manufacturing product candidates for clinical studies, and providing general and administrative support for these operations. To date, we have financed our operations primarily through the sale of equity securities. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations, or grants.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Our product candidates are in clinical development and we may never have a product candidate approved for commercialization. If we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidates may receive approval, and our ability to achieve sufficient market acceptance, pricing, reimbursement, and adequate market share for our product candidates in those markets. However, even if we obtain adequate market share for our product candidates, because the potential markets in which our product candidates may ultimately receive regulatory approval are very small, and our expenses may be greater than expected, we may never become profitable despite obtaining such market share and acceptance of our products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and nonclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- advance our programs into more expensive clinical studies;
- initiate additional nonclinical, clinical, or other studies for our product candidates;
- pursue preclinical and clinical development for additional indications for existing product candidates;
- change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- seek to identify, assess, license, acquire, and/or develop other product candidates, technologies and/or businesses;
- make milestone or other payments under any license agreements;
- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel;
- create additional infrastructure, including facilities and systems, to support the growth of our operations, our product development, and our planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above, including but not limited to failed studies, complex results, safety issues, inspections, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval.

Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

***We have never generated any revenue from product sales and may never be profitable.***

We have no products approved for commercialization and have never generated any revenue. Our ability to generate significant revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. We do not anticipate generating significant revenue from product sales in the near future. Our ability to generate substantial future revenue from product sales, including named patient sales, depends heavily on our success in many areas, including but not limited to:

- completing research and nonclinical and clinical development of our product candidates;
- obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies;
- developing a sustainable and scalable manufacturing process for any approved product candidates and establishing and maintaining supply and manufacturing relationships with third parties that can conduct the processes and provide adequate (in amount and quality) product supply to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our product candidates as viable treatment options;
- obtaining adequate reimbursement and pricing for our product candidates;
- our ability to sell our product candidates on a named patient basis or through an equivalent mechanism and the amount of revenue generated from such sales;
- addressing any competing technological and market developments;
- identifying, assessing, licensing, acquiring and/or developing new product candidates, technologies and/or businesses;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, the EMA, or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical, or other types of studies in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. For example, the development of KRN23, rhGUS, and UX007 for pediatric use is an important part of our current business strategy; if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

***We will likely need to raise additional capital to fund our activities. This additional financing may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product development efforts or other activities.***

We are currently advancing our KRN23, rhGUS, UX007, and Ace-ER product candidates through clinical development and our other product candidate, rhPPCA, as well as our other early stage research projects, through preclinical development. Developing our product candidates is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates through clinical studies and potential global commercialization.

As of December 31, 2015, our available cash, cash equivalents and investments were \$536.3 million. We will likely require additional capital to obtain regulatory approval for, and to commercialize, our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;

- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing field forces, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, acquisition, and other arrangements that we may establish, including any required milestone, royalty, and other payments thereunder.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through collaborative partnerships or other arrangements and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results, and prospects. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, and results of operations.

### **Risks Related to the Discovery and Development of Our Product Candidates**

***We are heavily dependent on the success of our product candidates, some of which are in the early stages of clinical development, which is a lengthy and expensive process with uncertain outcomes and the potential for substantial delays. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.***

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. To date, we have invested substantially all of our efforts and financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies and providing general and administrative support for these operations. We cannot be certain that any clinical studies will be conducted as planned or completed on schedule, if at all. Our inability to successfully complete nonclinical and clinical development could result in additional costs to us and negatively impact our ability to generate revenue. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We currently generate no revenue from sales of any drugs, and we may never be able to develop or commercialize a marketable drug. We cannot be certain that any of our product candidates will be successful in clinical studies or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in some clinical studies. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Each of our product candidates is in development and will require additional clinical development, management of nonclinical, clinical, and manufacturing activities, regulatory approval, obtaining adequate manufacturing supply, building of a commercial organization, significant marketing efforts, and reimbursement before we generate any significant revenue from commercial product sales. We currently have multiple programs that are in clinical studies. Three of our product candidates have advanced into pivotal studies, but such studies may not result in approval. For Ace-ER, we filed for conditional marketing authorization in the EU on the basis of results from our Phase 2 study, which study was originally designed to serve as a hypothesis-generating exploratory study and not as a pivotal study. Additionally, the study had a small sample size, did not have a primary endpoint and had a pre-specified unblinding that occurred halfway during the treatment period. Accordingly, the data from this Phase 2 study is not as comprehensive or robust as data that is typically generated from a pivotal Phase 3 study. Although conditional marketing authorization, initially allows for approval without providing comprehensive clinical data, marketing approval applications based on smaller and less definitive studies may entail a higher risk for rejection than the standard approval pathway. Even if we obtain conditional approval, it may be withdrawn under certain circumstances. In addition, confirmatory clinical studies would be required and could fail to demonstrate sufficient safety and efficacy to obtain full approval. We also currently plan to file for conditional marketing authorization for KRN23 for XLH in the EU. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates.

We cannot be certain that any of our product candidates will be successful in clinical studies or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical studies. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

We generally plan to seek regulatory approval to commercialize our product candidates in the United States, the EU, and in additional foreign countries where we have commercial rights. To obtain regulatory approval in other countries, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies, commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected.

Some of our product candidates are in the early-stage translational research phases of development. Such early-stage programs will require substantial investment to reach clinical studies and regulatory approval, and the risk of failure for them may be higher than with our clinical-stage product candidates. For example, our collaboration with Arcturus focuses on an advanced but less established technology platform that will require significant effort and investment. A failure in that collaboration or our other early-stage programs may negatively affect our operational results.

***The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable. Even if we achieve positive results in our pre-clinical and clinical studies, if we are ultimately unable to obtain timely regulatory approval for our product candidates, our business will be substantially harmed.***

Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. We have not obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

To obtain regulatory approval in the United States and other jurisdictions, we must comply with numerous and varying requirements regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies, commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development, which may cause delays in the approval or the decision not to approve an application. Communications with the regulatory agencies during the approval process are also unpredictable; favorable communications early in the process do not ensure that approval will be obtained and unfavorable communications early on do not guarantee that approval will not be obtained. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected. Applications for our product candidates could fail to receive regulatory approval, or could be delayed in receiving regulatory approval, for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical studies;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of an NDA, or BLA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- as a condition of marketing authorization in the EU, an agreed upon Pediatric Investigational Plan (PIP) detailing the designs and completion timelines for nonclinical and clinical studies is required. If the nonclinical or clinical development does not comply with the agreed upon PIP, marketing authorization could be denied or significantly delayed; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Furthermore, the disease states we are evaluating often will not have clear regulatory paths for approval and/or do not have validated outcome measures. In these circumstances, we work closely with the regulatory authorities to define the approval path and may have to qualify outcome measures as part of our development programs. For example, for patients with XLH there is no available regulatory precedent for what is needed to obtain approval to treat this disease and there are no validated patient-reported outcome measures that are specific to this disease. Additionally, many of the disease states we are targeting are highly heterogeneous in nature, which may impact our ability to determine the treatment benefit of our potential therapies. For example, patients with FAOD and MPS 7 have a highly heterogeneous disease course, which may impact our ability to determine the true treatment benefit of our product candidates in these patients.

This lengthy and uncertain approval process, as well as the unpredictability of the clinical and nonclinical studies, may result in our failing to obtain regulatory approval to market any of our product candidates, or being delayed in obtaining regulatory approval, which would significantly harm our business, results of operations, and prospects.

***Clinical drug development involves a lengthy and expensive process with uncertain outcomes and the potential for substantial delays, and the results of earlier studies may not be predictive of future study results.***

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time consuming, and uncertain as to outcome. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Product candidates that have shown promising results in early-stage clinical studies may still suffer significant setbacks in subsequent clinical studies. For example, the safety or efficacy results generated to date in clinical studies for KRN23, rhGUS, UX007, and Ace-ER do not ensure that later clinical studies will demonstrate similar results. Results from investigator-sponsored studies or compassionate-use studies may not be confirmed in company-sponsored studies or may negatively impact the prospects for our programs. Additionally, given the nature of the rare diseases we are seeking to treat, we often have to devise newly-defined endpoints to be tested in our studies, which can lead to some subjectivity in interpreting study results and could result in regulatory agencies not agreeing with the validity of our endpoints, or our interpretation of the clinical data, and therefore denying approval. Given the illness of the subjects in our studies and the nature of their rare diseases, we may also be required or choose to conduct certain studies on an open-label basis. Additionally, we have in the past, and may in the future elect to or we might review interim clinical data at multiple time points during the studies, which could introduce bias into the study results.

In the biopharmaceutical industry, there is a high failure rate for drugs and biologics proceeding through clinical studies, and product candidates in later stages of clinical studies may fail to show the desired safety and efficacy despite having progressed through nonclinical studies and initial clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical studies due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies.

Scenarios that may prevent successful or timely completion of clinical development include but are not limited to:

- our inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of human clinical studies or filings for regulatory approval;
- delays or failures in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations (or CROs), clinical study sites, and other clinical trial-related vendors;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical study site;
- changes in clinical study design or development strategy resulting in delays related to obtaining approvals from IRBs and/or regulatory agencies to proceed with clinical studies;
- failure to gain approval from regulatory authorities or IRBs to conduct clinical studies in certain countries;
- imposition of a clinical hold by regulatory agencies after review of an IND application or amendment, another equivalent application or amendment, or an inspection of our clinical study operations or study sites;
- delays in recruiting suitable patients to participate in our clinical studies;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's good clinical practices requirements or applicable regulatory guidelines in other countries;
- delays in patients' completion of studies or their returns for post-treatment follow-up;
- patients dropping out of a study;

- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- the cost of clinical studies of our drug candidates being greater than we anticipate;
- clinical studies of our drug candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring us, to conduct additional clinical or nonclinical studies or to abandon drug development programs;
- competing clinical studies of potential alternative product candidates or investigator-sponsored studies of our product candidates; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing.

Any inability to successfully complete nonclinical and clinical development could result in additional costs to us or negatively impact our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, such as our plan to manufacture a combination extended release and immediate release version of sialic acid, or new formulations of UX007, we may need to conduct additional studies to bridge our modified product candidates to earlier approved versions. Clinical study delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could negatively impact our ability to obtain orphan exclusivity and to successfully commercialize our product candidates and may harm our business and results of operations.

***We may find it difficult to enroll patients in our clinical studies given the limited number of patients who have the diseases for which our product candidates are being studied. Difficulty in enrolling patients could delay or prevent clinical studies of our product candidates.***

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical studies if we encounter difficulties in enrollment.

Each of the conditions for which we plan to evaluate our current product candidates is a rare genetic disease. Accordingly, there are limited patient pools from which to draw for clinical studies. For our current product candidates:

- we estimate that several thousand patients in the United States suffer from XLH, for which KRN23 is being studied;
- we estimate that several hundred patients in the United States suffer from TIO, for which KRN23 is being studied;
- we estimate that up to approximately 200 patients in the developed world may suffer from MPS 7, for which rhGUS is being studied;
- we estimate that several thousand patients in the United States suffer from LC-FAOD, for which UX007 is being studied;
- we estimate that several thousand patients in the United States suffer from Glut1 DS, for which UX007 is being studied; and
- we estimate that approximately 2,000 patients in the developed world suffer from GNE myopathy, for which Ace-ER is being studied.

In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. For example, the UX007 Glut1 DS Phase 2 study requires a certain minimum baseline rate of generalized tonic-clonic seizures or the presence of absence seizures at baseline. Additionally, the process of finding and diagnosing patients may prove costly. We also may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidate under study, the proximity and availability of clinical study sites for prospective patients, and the patient referral practices of physicians. The availability and efficacy of competing therapies and clinical studies can also adversely impact enrollment. For example, our Phase 2 UX007 Glut1 DS study is enrolling patients who are not currently on or compliant with the ketogenic diet. However, the ketogenic diet is the standard of care and considered effective in seizure control. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented. In addition, any delays in completing our clinical studies will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition, and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates.

***If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.***

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials, the submission of regulatory filings, and the potential approval of such regulatory filings. We periodically make public announcements about the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions, but the actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

***Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.***

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies or further development, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Some of our product candidates are in the early stages of development and the safety profile has not been established. For example, in the completed Phase 1 study, four-month Phase 1/2 study, and long-term twelve-month Phase 1/2 study, adult patients treated with KRN23 have experienced drug-related side effects including injection site reaction, arthralgia, diarrhea, restless legs syndrome, injection site erythema, injection site pain, upper abdominal pain, headache and decreased neutrophil count. Most of these adverse events were mild and no treatment-related serious adverse events have been observed. In interim Phase 2 data in pediatric patients, the most common treatment related adverse event by preferred term was injection site reaction. There were no deaths and there was one serious adverse event of fever and muscle pain in a patient that was considered possibly treatment related. Patients treated with triheptanoin have experienced drug-related side effects such as cramping, diarrhea, and loose stools. In addition, over 14 years of treatment experience in approximately 130 human subjects, including greater than 60 with LC-FAOD, we are aware of three serious adverse events that were classified as possibly related to triheptanoin treatment (muscle cell rupture and elevated creatine kinase reported for two subjects and myoglobinuria in one subject); however, these serious adverse events can be considered typical of the underlying disease. In interim data from our Phase 2 study there were no deaths but there was one treatment related serious adverse event of moderate gastroenteritis with vomiting. The most common treatment-related adverse events were diarrhea, abdominal/gastrointestinal pain, and vomiting. While we have not completed our own clinical studies for UX007, there may be other side effects associated with its use that we discover. Additionally, patients treated with Ace-ER have experienced drug-related side effects including mild gastrointestinal discomfort. Enzyme replacement therapies have been associated with infusion-associated reactions due to a developing allergy to the product, which can cause rashes, pain, significant clinical disease, or even death. Our rhGUS and rhPPCA product candidates may also cause these or similar side effects as further development proceeds. Results of our studies or investigator-sponsored trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our studies could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny or withdraw approval of our product candidates for any or all targeted indications.

Drug-related side effects could affect patient recruitment and the ability of enrolled patients to complete the study. Such side effects could also or result in potential product liability claims. We currently carry product liability insurance in the amount of \$10.0 million per incident and \$10.0 million in the aggregate, and we are required to maintain product liability insurance pursuant to certain of our agreements. We believe our product liability insurance coverage is sufficient in light of our current clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability, or losses may exceed the amount of insurance that we carry. A product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical study participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the product's label or restrict the product's approved use;
- we may be required to create a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, restricted distribution, a communication plan for healthcare providers, and/or other elements to assure safe use;

- we could be sued and held liable for harm caused to patients;
- patients and physicians may elect not to use our products, or reimbursement authorities may elect not to reimburse for them; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

***Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.***

If our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, distribution, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority, requirements, including ensuring that quality control and manufacturing procedures conform to GMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspection to assess compliance with GMP and adherence to commitments made in any NDA, BLA, MAA, or other comparable application for approval in another jurisdiction. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical studies, and surveillance to monitor the safety and efficacy of the product candidate. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval were obtained via the accelerated approval or conditional marketing authorization pathways, we would be required to conduct a successful post-marketing clinical study to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will be required to report certain adverse events and manufacturing problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, MAA, or other comparable application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process.

If we fail to comply with applicable regulatory requirements, or there are safety or efficacy problems with a product, a regulatory agency or enforcement authority may, among other things:

- issue warning or notice of violation letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain products, or require a product recall; or
- require entry into a consent decree.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

***Changes in methods of treatment of disease could reduce demand for our products and adversely affect revenues.***

Even if our drug products are approved, if doctors elect a course of treatment which does not include our drug products, this decision would reduce demand for our drug products and adversely affect revenues. Changes in treatment method can be caused by the introduction of other companies' products or the development of new technologies or surgical procedures which may not directly compete with ours, but which have the effect of changing how doctors decide to treat a disease.

**Risks Related to our Reliance on Third Parties**

***We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may be exposed to sub-optimal quality and reputational harm, we may not be able to obtain regulatory approval for or commercialize our product candidates, and our business could be substantially harmed.***

We have relied upon and plan to continue to rely upon third parties, including CROs and collaborative partners, to analyze, collect, monitor and manage data for our ongoing nonclinical and clinical programs. We rely on third parties for execution of our nonclinical and clinical studies, and for estimates regarding costs and efforts completed, and we control only certain aspects of their activities. For example, we will rely on our partner Arcturus for the design and optimization of initial product candidates under our messenger RNA collaboration. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs and other vendors and partners are required to comply with GMP, GCP, and GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the EEA, and comparable foreign regulatory authorities for all of our product candidates in development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, and other contractors. If we or any of our CROs or other vendors and partners fail to comply with applicable regulations, the data generated in our nonclinical and clinical studies may be deemed unreliable and the FDA, EMA, or comparable foreign regulatory authorities may require us to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the approval process. We cannot make assurances that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with GCP regulations or that nonclinical studies comply with GLP regulations. In addition, our clinical studies must be conducted with products produced under GMP regulations. If we fail to comply with these regulations, we may be required to repeat clinical or nonclinical studies, which would delay the regulatory approval process.

Our CROs and other vendors and partners are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our on-going nonclinical and clinical programs. If our vendors and partners do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical studies may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs and other vendors and partners may also generate higher costs than anticipated as a result of changes in scope of work or otherwise. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative vendors or do so on commercially reasonable terms. Switching or adding additional vendors involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new vendor commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our vendors and partners, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and business prospects.

We also rely on third parties in other ways, including to support our patient identification efforts, to assist our finance and legal departments, and to provide other resources for our business. Use of these third parties could expose us to sub-optimal quality, missed deadlines, and non-compliance with applicable laws, all of which could result in reputational harm to us and negatively affect our business.

***We are dependent on KHK for the clinical and commercial supply of KRN23 for all major markets and for the development and commercialization of KRN23 in certain major markets, and KHK's failure to provide an adequate supply of KRN23 or to commercialize KRN23 in those markets could result in a material adverse effect on our business and operating results.***

Under our agreement with KHK, KHK has the sole right to commercialize KRN23 in Europe and, at a specified time, in the United States and Canada subject to a limited promotion right we retained. Our development partnership with KHK may not be successful, and we may not realize the expected benefits from such partnership, due to a number of important factors, including but not limited to the following:

- KHK has no obligation under our agreement to use diligent efforts to commercialize KRN23 in Europe. The timing and amount of any royalty payments we may receive under our agreement will depend on, among other things, the efforts, allocation of resources, and successful commercialization of KRN23 by KHK in Europe. Additionally, if KHK were to decide not to commercialize KRN23 in Europe, and we nevertheless wished to commercialize KRN23 in Europe, we would need to renegotiate with KHK certain terms of our agreement, which we may be unable to do on reasonable terms in a timely manner, or at all;
- the timing and amount of any royalty payments we may receive under our agreement with KHK will depend on, among other things, the efforts, allocation of resources, and successful commercialization of KRN23 by KHK in the United States and Canada under our agreement;
- KHK may change the focus of its commercialization efforts or pursue higher-priority programs;
- KHK may fail to manufacture or supply sufficient drug product of KRN23 in compliance with applicable laws and regulations or otherwise for our development and clinical use, which could result in program delays;
- KHK may fail to manufacture or supply sufficient drug product of KRN23 in compliance with applicable laws and regulations or otherwise for our commercial use, if approved, which could result in lost revenue;
- KHK may elect to develop and commercialize KRN23 indications with a larger market than XLH and at a lower price, thereby reducing the profit margin on sales of KRN23 for any orphan indications, including XLH;
- if KHK were to breach or terminate the agreement with us, we would no longer have any rights to develop or commercialize KRN23 or such rights would be limited to non-terminated countries;
- KHK may terminate its agreement with us, adversely affecting our potential revenue from licensed products; and
- the timing and amounts of expense reimbursement that we may receive are uncertain, and the total expenses for which we are obligated to reimburse KHK may be greater than anticipated.

***We rely completely on third parties to manufacture our product candidates. Our business could be harmed if those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices.***

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our product candidates, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a limited number of suppliers for raw materials that we use to manufacture our drugs, placebos, or active controls, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Although we generally do not begin a clinical study unless we believe we have a sufficient supply of a product candidate to complete such study, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical study due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing, and potential regulatory approval of our product candidates, and could also impair named patient sale supply of our product candidates, which could harm our business and results of operations.

***We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit supply of our product candidates.***

The process of manufacturing our product candidates is complex, highly regulated, and subject to several risks, including but not limited to:

- the process of manufacturing our product candidates is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes for any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination; and
- the manufacturing facilities in which our product candidates are made could be adversely affected by equipment failures, labor shortages, raw material shortages, natural disasters, power failures, and numerous other factors.

Although we have not experienced any significant manufacturing problems, any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our product candidates. We may also have to take inventory write-offs and incur other charges and expenses for product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

***The drug substance and drug product for most of our product candidates are currently acquired from single-source suppliers. The loss of these suppliers, or their failure to supply us with the drug substance or drug product, could materially and adversely affect our business.***

The drug substance and drug product for KRN23 are made by KHK pursuant to our license and collaboration agreement with KHK. The drug substance and drug product for rhGUS are manufactured by Rentschler Biotechnologie GmbH under a development and clinical supply agreement and accompanying purchase orders. The pharmaceutical-grade drug substance for UX007 is manufactured by Cremer Oleo GmbH & Co. KG, or Cremer, pursuant to our supply agreement with Cremer, and the drug product for UX007 is prepared by Haupt Pharma AG and CPM pursuant to purchase orders. The drug substance for Ace-ER is manufactured by Sanyo Fine Co., Ltd. under our license agreement and accompanying purchase orders with Nobelpharma Co., Ltd. and under our clinical supply agreement with Evonik Corporation, and the drug product for Ace-ER is manufactured by AAIPharma Services Corp., or AAIPharma, pursuant to our license agreement and accompanying purchase orders with AAIPharma. We have not currently secured any other suppliers for the drug substance or drug product of our product candidates and, although we believe that there are alternate sources of supply that could satisfy our clinical and commercial requirements, we cannot provide assurance that identifying alternate sources and establishing relationships with such sources would not result in significant delay in the development of our product candidates. Additionally, we may not be able to enter into supply arrangements with alternative suppliers on commercially reasonable terms or at all. A delay in the development of our product candidates or having to enter into a new agreement with a different third-party on less favorable terms than we have with our current suppliers could have a material adverse impact upon our business.

***We and our collaborators and contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.***

All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical studies must be manufactured in accordance with GMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We, our collaborators, or our contract manufacturers must supply all necessary documentation in support of an NDA, BLA, MAA, or other application for regulatory approval, on a timely basis and must adhere to GLP, GMP, and similar regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our collaborators and third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are substantially dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our collaborators and third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third-party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we, our collaborators, or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, withdrawal of an approval, or suspension of production. As a result, our business, financial condition, and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA or BLA supplement or MAA variation, or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical studies, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we rely on third parties to develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements, letters of engagement, or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

## Risks Related to Commercialization of Our Product Candidates

***If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our product candidates are small, and the addressable patient population potentially even smaller, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.***

We focus our research and product development on treatments for rare and ultra-rare genetic diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare and ultra-rare genetic diseases. Some of our current clinical programs may be most appropriate for patients with more severe forms of their disease. For instance, our Phase 2 study of UX007 in LC-FAOD enrolled patients with more severe disease. In addition, while adults make up the majority of the XLH patients, they often have less severe disease which may reduce the penetration of KRN23 in the adult population relative to the pediatric population. Given the overall rarity of the diseases we target, it is difficult to project the prevalence of the more severe forms, or the other subsets of patients that may be most suitable to address with our product candidates, which may further limit the addressable patient population to a small subset. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small we may never become or remain profitable nor generate sufficient revenue growth to sustain our business.

***We intend to rely on third-party manufacturers to produce our product candidates, but we have not entered into binding agreements with any such manufacturers to support commercialization. Additionally, these manufacturers do not have experience producing our product candidates at commercial levels and may not achieve the necessary regulatory approvals or produce our product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization.***

We have not yet secured manufacturing capabilities for commercial quantities of our product candidates. Although we intend to rely on third-party manufacturers for commercialization, we have only entered into agreements with such manufacturers to support our clinical studies. We may be unable to negotiate binding agreements with the manufacturers to support our commercialization activities on commercially reasonable terms.

Manufacturers may not have the experience or ability to produce our product candidates at commercial levels. We may run into technical or scientific issues related to manufacturing or development that we may be unable to resolve in a timely manner or with available funds. We also have not completed all of the characterization and validation activities necessary for commercialization and regulatory approvals. If our manufacturing partners are not able to conduct all such necessary activities in accordance with applicable regulations, our commercialization efforts will be harmed.

Even if our third-party product manufacturers develop an acceptable manufacturing process, if such third-party manufacturers are unable to produce the necessary quantities of our product candidates, or in compliance with GMP or other pertinent regulatory requirements, and within our planned timeframe and cost parameters, the development and sales of our products, if approved, may be materially harmed.

Even if our third-party product manufacturers develop acceptable manufacturing processes that provide the necessary quantities of our product candidates in a compliant and timely manner, the cost to us for the supply of our product candidates by such third-parties may be high and limit our profitability. Furthermore, KHK is our sole supplier of commercial quantities of KRN23. The supply price to us for commercial sales of KRN23, which will be determined on a fixed double-digit percentage of net sales, will be higher than the typical cost of goods sold by companies focused on rare diseases.

***We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are similar, more advanced, or more effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates.***

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing therapies that may compete with our product candidates. For example, XLH is currently treated with oral phosphate and Vitamin D therapy, which may compete with KRN23. Furthermore, B. Braun Medical Inc., or B. Braun, has received orphan drug designation for triheptanoin in Europe for certain LC-FAOD indications and we do not know if B. Braun is planning to initiate clinical development. Triheptanoin is also available in food-grade form, which may compete with our pharmaceutical-grade product. Investigator-sponsored trials evaluating triheptanoin in multiple indications are ongoing. LC-FAOD is currently treated with diet therapy and medium-chain triglyceride oil, which may compete with UX007. Glut1 DS is currently treated primarily with the ketogenic diet and anti-epileptic drugs, which may also compete with UX007. Additionally, we are aware of a program at the National Institutes of Health that is investigating the use of another metabolite in the sialic acid pathway, ManNAc, for the treatment of GNE myopathy, which could compete with Ace-ER. The intellectual property rights for ManNAc are licensed to Escala Therapeutics, a subsidiary of Fortress Biotech, Inc., which acquired the rights from a company in New Zealand that manufactures ManNAc. ManNAc may have a potential advantage over Ace-ER in that it is not a charged molecule like sialic acid is, which might improve its distribution and uptake. Gene therapy, gene correction, RNA-based therapies, and other approaches may also emerge for the treatment of any of the disease areas in which we focus.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. Some of the pharmaceutical and biotechnology companies we expect to compete with include Shire, Sanofi, BioMarin, Alexion, and Roche, as well as other companies ranging from startups to large multinational companies. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring, or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization, and market penetration than we do. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

***We are currently building an integrated commercial organization. If we are unable to establish sufficient field forces and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.***

Although our employees may have sold other similar products in the past while employed at other companies, we as a company have no experience selling and marketing our product candidates and we currently have minimal marketing and field force capacity. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. If our product candidates receive regulatory approval, we intend to establish marketing organization and field forces with technical expertise as well as supporting distribution capabilities to commercialize our product candidates in major markets, which will be expensive, difficult, and time consuming. Any failure or delay in the development of our internal field forces, marketing, and distribution capabilities would adversely impact the commercialization of our products.

Further, given our lack of prior experience in marketing and selling biopharmaceutical products, our initial estimate of the size of the required field force may be materially more or less than the size of the field force actually required to effectively commercialize our product candidates. As such, we may be required to hire large teams to adequately support the commercialization of our product candidates or we may incur excess costs as a result of hiring more sales field personnel than necessary. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We may be competing with companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third-party to perform key commercial functions, we may be unable to compete successfully against these more established companies.

***The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.***

Even with the requisite approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our product candidates will depend in part on the medical community, patients, and payors accepting our product candidates as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, payors, and others in the medical community. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the clinical indications for which approval is granted;
- relative convenience and ease of administration;
- the cost of treatment, particularly in relation to competing treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of our field forces and marketing efforts;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in nonclinical and clinical studies, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and payors on the benefits of the product candidates may require significant resources and may never be successful. If our product candidates are approved but fail to achieve an adequate level of acceptance by physicians, patients, payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

***The insurance coverage and reimbursement status of newly approved products is uncertain. 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.***

Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of our product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford expensive treatments such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other payors. If coverage and reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for products such as ours.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries will put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. For example, within the last year, several states in the U.S. have introduced legislation to require pharmaceutical companies to disclose their costs to justify the prices of their products, and an “Affordable Drug Pricing Task-Force” has been formed in the U.S. House of Representatives with the goal of combating the increased costs of prescription drugs. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

### **Risks Related to Our Intellectual Property**

***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.***

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies and product candidates. Our success depends in large part on our and our licensors’ ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and products.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

We, independently or together with our licensors, have filed several patent applications covering various aspects of our product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

Although we have a number of patents or applications covering methods of use and certain compositions of matter, we do not have complete patent protection for our product candidates. For example, there are no issued patents and very limited pending applications for KRN23 in Latin America, where we have rights to commercialize the compound. Therefore, a competitor could develop the same or similar antibody as well as other approaches that target FGF23. Additionally, there are currently no issued patents that cover rhGUS or rhPPCA. Therefore, it is possible that a competitor could develop the same or similar enzyme with respect to rhGUS or rhPPCA, subject to any regulatory exclusivities. With respect to Ace-ER, none of the patents or applications relating to Ace-ER cover composition of matter. Therefore, it is possible that a competitor could develop the same or similar molecule. If we cannot obtain and maintain effective patent rights for our product candidates, we may not be able to compete effectively and our business and results of operations would be harmed.

***We may not have sufficient patent terms to effectively protect our products and business.***

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

While patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend the patent exclusivity term for KRN23, rhGUS, UX007, and Ace-ER, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. In addition, upon issuance in the United States any patent term can be adjusted based on certain delays caused by the applicant(s) or the USPTO. For example, a patent term can be reduced based on certain delays caused by the patent applicant during patent prosecution. If we do not have sufficient patent terms or regulatory exclusivity to protect our products, our business and results of operations will be adversely affected.

***Patent policy and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.***

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. We therefore cannot be certain that we or our licensors were the first to make the invention claimed in our owned and licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions. Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, enacted on September 16, 2011, the United States has moved to a first to file system. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and may also affect patent litigation. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address any of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. In general, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

***If we are unable to maintain effective proprietary rights for our product candidates or any future product candidates, we may not be able to compete effectively in our markets.***

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

***Claims of intellectual property infringement may prevent or delay our development and commercialization efforts.***

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of others. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by other parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of these other parties.

Other parties may assert that we are employing their proprietary technology without authorization. There may be patents or patent applications with claims to materials, formulations, methods of manufacture, or methods for treatment related to the use or manufacture of our product candidates. We have conducted freedom to operate analyses with respect to only certain of our product candidates, and therefore we do not know whether there are any patents of other parties that would impair our ability to commercialize all of our product candidates. We also cannot guarantee that any of our analyses are complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. For example, we are aware of a pending U.S. patent application by the Japan Health Sciences Foundation. Although we do not believe any valid and enforceable claim covering our product candidate will be issued from this U.S. application, we cannot guarantee that such claim will not issue.

In addition, other parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any of these patents were held by a court of competent jurisdiction to cover aspects of our formulations, the manufacturing process of any of our product candidates, methods of use, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

***We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.***

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

***We may face competition from biosimilars, which may have a material adverse impact on the future commercial prospects of KRN23, rhGUS, and rhPPCA.***

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars with respect to KRN23, rhGUS, and rhPPCA. In the United States, the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, created an abbreviated approval pathway for biological products that are demonstrated to be “highly similar,” or biosimilar, to or “interchangeable” with an FDA-approved biological product. The BPCI Act prohibits the FDA from approving a biosimilar or interchangeable product that references a brand biological product until 12 years after the licensure of the reference product, but permits submission of an application for a biosimilar or interchangeable product to the FDA four years after the reference product was first licensed. The BPCI Act does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. In the budget for fiscal year 2016, the Obama administration reasserted its proposal from prior years to cut this 12-year period of exclusivity down to seven years. The administration also reasserted a proposal to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as “evergreening.” In October 2015, the United States agreed to the Trans-Pacific Partnership (TPP), an agreement with 11 other countries that addresses a variety of trade and economic issues. The TPP includes a provision that would require the signatory countries to provide a minimum of five years of exclusivity, and in some instances, eight years of exclusivity, to biological products. To come into effect, the TPP will require a requisite number of signatory countries to ratify the agreement; in the United States, such ratification, if it occurs, will be performed by Congress. It is possible that Congress could seek to harmonize the exclusivity periods in the TPP and the BPCI Act, or take other measures to modify or eliminate periods of exclusivity for biosimilar and interchangeable products. The BPCI Act is complex and is only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning is subject to uncertainty. Changes to the BPCI Act or the FDA’s interpretation or implementation of the BPCI Act could have a material adverse effect on the future commercial prospects for KRN23, rhGUS, and rhPPCA.

In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products.

If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

***Additional competitors could enter the market with generic versions of our small-molecule product candidates, which may result in a material decline in sales of UX007 and Ace-ER.***

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA’s finding of safety and effectiveness of a previously approved drug. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. Innovative small molecule drugs may be eligible for certain periods of regulatory exclusivity (e.g., five years for new chemical entities, three years for changes to an approved drug requiring a new clinical study, seven years for orphan drugs), which preclude FDA approval (or in some circumstances, FDA filing and review of) an ANDA or 505(b)(2) NDA relying on the FDA’s finding of safety and effectiveness for the innovative drug. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the “Orange Book.” If there are patents listed in the Orange Book, a generic applicant that seeks to market its product before expiration of the patents must include in the ANDA or 505(b)(2) what is known as a “Paragraph IV certification,” challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if UX007 and Ace-ER are approved, competitors could file ANDAs for generic versions of UX007 and Ace-ER, or 505(b)(2) NDAs that reference UX007 and Ace-ER, respectively. If there are patents listed for UX007 and Ace-ER in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict whether any patents issuing from our pending patent applications will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could more immediately face generic competition and its sales would likely decline materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected.

***The patent protection and patent prosecution for some of our product candidates is dependent on third parties.***

While we normally seek and gain the right to fully prosecute the patents relating to our product candidates, there may be times when patents relating to our product candidates are controlled by our licensors. This is the case with our agreement with KHK, who is primarily responsible for the prosecution of patents and patent applications licensed to us under the collaboration agreement. If KHK or any of our future licensing partners fail to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to us assuming control over patent prosecution.

***If we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.***

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license. Additionally, the milestone and other payments associated with these licenses will make it less profitable for us to develop our drug candidates. See “Business—License Agreements” for a description of our license agreements with KHK, Baylor Research Institute, Nobelpharma, AAIPharma, HIBM Research Group, St. Louis University, and St. Jude Children’s Research Hospital, which includes a description of the termination provisions of these agreements.

In some cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding intellectual property subject to a licensing agreement, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and
- the priority of invention of patented technology.

If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

***Although we are not currently involved in any litigation, we may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful.***

Competitors may infringe our patents or the patents of our licensors. Although we are not currently involved in any litigation, if we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise sufficient capital to continue our clinical studies, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

***We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

We employ certain individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of others in their work for us, and we are not currently subject to any claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties, we may in the future be subject to such claims. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***We may be subject to claims challenging the inventorship of our patents and other intellectual property.***

Although we are not currently experiencing any claims challenging the inventorship of our patents or ownership of our intellectual property, we may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity. Therefore, obtaining and enforcing biotechnology patents is costly, time consuming, and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty about our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

***We may not be able to protect our intellectual property rights throughout the world.***

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Further, licensing partners such as KHK may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

**Risks Related to Our Business Operations**

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

We are dependent on Emil D. Kakkis, M.D., Ph.D., our Founder, President, and Chief Executive Officer, the loss of whose services may adversely impact the achievement of our objectives. Dr. Kakkis could leave our employment at any time, as he is an “at will” employee. Recruiting and retaining other qualified employees, consultants, and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis, may impede the progress of our research, development, and commercialization objectives.

***If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced.***

Our business strategy focuses on the development of drugs that are eligible for FDA and EU orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the EMA’s Committee for Orphan Medicinal Products for Human Use grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition when the prevalence of the condition is not more than five in 10,000 persons in the EU or when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product. Additionally, there must be no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Because the extent and scope of patent protection for our products may in some cases be limited, orphan drug designation is especially important for our products for which orphan drug designation may be available. For eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products and biologic products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity and our revenue will be reduced.

Even though we have orphan drug designation for UX007 for the treatment of fatty acid oxidation disorders in the United States, as well as for UX007 for the treatment of Glut1 DS, KRN23, rhGUS and Ace-ER in the United States and Europe, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition or the same drug can be approved for a different indication unless there are other exclusivities such as new chemical entity exclusivity preventing such approval. Even after an orphan drug is approved, the FDA or EMA can subsequently approve the same drug with the same active moiety for the same condition if the FDA or EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

***We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.***

As of December 31, 2015, we had 249 full-time employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, field forces, marketing, financial, legal, and other resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

***We may not be successful in our efforts to identify, license, discover, develop, or commercialize additional product candidates.***

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval, and commercialization of our existing product candidates, the success of our business also depends upon our ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify and develop new product candidates, such as those under our collaboration with Arcturus, requires substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- we may face competition in obtaining and/or developing additional product candidates;
- our product candidates may not succeed in preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost or at all; and
- a product candidate may not be accepted as safe and effective by regulatory authorities, patients, the medical community, or payors.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, or we may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations.

***We incur increased costs as a result of operating as a public company, and our management is now required to devote substantial time to new compliance initiatives and corporate governance practices.***

As a public company, we incur significant legal, accounting, and other expenses. Until December 31, 2015, we were eligible for reduced reporting and disclosure requirements as an “emerging growth company.” We are no longer an “emerging growth company” and, accordingly, we are required to comply with several supplemental requirements that will necessitate additional resources and management time and expense. These supplemental requirements include providing full executive compensation disclosure, such as Compensation, Discussion & Analysis section in our proxy statement for the annual meeting of stockholders; a say-on-frequency vote; a say-on-pay vote beginning with this year’s Annual Meeting of Stockholders; and pay-ratio disclosure beginning with our 2018 Annual Meeting of Stockholders. We will also be subject to rules subsequently implemented by the SEC and The NASDAQ Global Select Market. In addition, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities more time consuming and costly. For example, being a public company could make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain adequate levels of such coverage.

Additionally, the Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404(a) of the Sarbanes-Oxley Act. We are now also subject to the compliance requirements of Section 404(b) of the Sarbanes-Oxley Act, which has resulted in us incurring substantial expenses and expending significant management efforts to comply with the Act, which we will continue. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we are not able to comply with the requirements of Section 404(b) or if we identify or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC, or other regulatory authorities, which would require additional financial and management resources.

***Changes to healthcare and FDA laws, regulations and policies may have a material adverse effect on our business and results of operations.***

*United States*

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs and to modify the regulation of drug and biologic products. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The PPACA, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and promotes a new Medicare Part D coverage gap discount program.

The Consolidated Appropriations Act, signed into law on December 18, 2015, modifies certain provisions of the PPACA; the new appropriations law suspends or delays several taxes, including the excise tax on high cost employer-sponsored health coverage, which were expected to generate significant funds for the PPACA. Implementation of the PPACA remains ongoing, and there remains uncertainty as to how the law’s various provisions will ultimately affect the industry.

In addition, other legislative changes have been adopted in the United States to contain healthcare costs. On August 2, 2011, the Budget Control Act of 2011, among other things, required reductions in federal spending, which eventually triggered Medicare sequestration—the requirement to reduce Medicare payments to providers up to 2% per fiscal year. Following an executive order by President Obama on March 1, 2013, the 2% Medicare payment reductions were applied to fee-for-service claims with dates of service or dates of discharge on or after April 1, 2013. Sequestration was initially set to expire in fiscal year 2021 but was extended, most recently by the Bipartisan Budget Act of 2015, which extends Medicare sequestration to 2025. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, and which could result in reduced demand for our product candidates or additional pricing pressures.

In addition, the FDA's laws, regulations, and policies remain the subject of agency and legislative proposals for reform, which could affect our product development, testing, marketing approvals, and post-market activities. For example, as discussed in the risk factor entitled "***We may face competition from biosimilars, which may have a material adverse impact on the future commercial prospects of KRN23, rhGUS, and rhPPCA***", there are proposals to reduce the exclusivity protections provided to biosimilar and interchangeable biologic products, and FDA has begun to issue policies regarding key aspects of the regulation of these products. Congress also is considering various proposals relating to FDA's premarket approval process and other issues. For example, the 21st Century Cures Act, which passed the U.S. House of Representatives in July 2015, proposes a wide range of reforms, such as broadening the types of data required to support drug approval, extending protections from genetic competition, accelerating approval of breakthrough therapies, expanding the orphan drug product program, and clarifying how manufacturers communicate about their products. It is uncertain whether these or similar proposals will be passed into law.

#### European Union

In the EU, the European Commission adopted the Commission Delegated Regulation (EU) No 2016/161 of 2 October 2015, supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use. The Regulation lays down the rules for the features appearing on the packaging of these medicinal products, including, inter alia, the characteristics and technical specifications of the unique identifier that enables the authenticity of medicinal products to be verified and individual packs to be identified, the modalities for the verification of the safety features, and the list of medicinal products and product categories subject and not subject to prescription which shall not bear and bear (respectively) safety features.

The European Commission has also launched a series of public consultations that are aimed to the adoption of Notices and Guidelines which will serve the interpretation of currently applicable Regulations and Directives.

For example, from August 28, 2015 with closing date November 24, 2015 the European Commission launched four public consultations which concerned good manufacturing practices and clinical trials for human medicinal products. From November 16, 2015 to February 15, 2016, the European Commission opened a public consultation from the Commission on certain aspects of the application of Articles 3, 5 and 7 of Regulation (EC) No 141/2000 on orphan medicinal products. The purpose of the Consultation is to review the 2003 Communication on orphan medicinal products (which will be replaced with a Notice), in order to streamline the regulatory framework and to adapt the Communication to technical progress. The consultation focuses on a variety of elements of Regulation (EC) No 141/2000, which include the encouragement of development of orphan medicinal products for communicable diseases and the simplification of the procedure for the reassessment of orphan criteria when two authorization application procedures are pending in parallel for two orphan medicinal products.

***We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed field, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other payors that are false or fraudulent; HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

- HIPAA, as amended by HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the PPACA requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any payor, including commercial insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the PPACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

***International expansion of our business exposes us to business, regulatory, political, operational, financial, and economic risks associated with doing business outside of the United States.***

We currently have limited international operations, but our business strategy incorporates potentially significant international expansion, particularly in anticipation of approval of our product candidates. We currently conduct physician and patient association outreach activities, as well as clinical studies, outside of the United States and plan to maintain field forces representatives internationally in the future. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- introductions of new Health Authority requirements and/or changes in Health Authority expectations;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters and political and economic instability, including wars, terrorism, political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance;

- regulatory and compliance risks that relate to maintaining accurate information and control over commercial operations and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, its books and records provisions, or its anti-bribery provisions; and
- regulatory and compliance risks relating to doing business with any entity that is subject to sanctions administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

***We may incur additional tax liabilities related to our operations.***

We are subject to income tax in the United States and various foreign jurisdictions. Significant judgment is required in determining our worldwide tax liabilities, and our effective tax rate is derived from a combination of the applicable statutory rates in the various jurisdictions in which we operate. We record liabilities that involve significant management judgment for uncertain tax positions. The IRS or other domestic or foreign taxing authorities may disagree with our interpretation of tax law as applied to the operations of Ultragenyx or with the positions we may take with respect to particular tax issues on our tax returns. Consequently, our reported effective tax rate and our after-tax cash flows may be materially and adversely affected by tax assessments or judgments in excess of accrued amounts we have estimated in preparing our financial statements. Further, our effective tax rate may also be adversely affected.

Our effective tax rate is derived from a combination of the applicable statutory rates in the various jurisdictions in which we operate. Such rate may be adversely affected by numerous factors, including changes in our operating structure, changes in the mix of our earnings among countries with differing statutory rates, including those resulting from our intercompany transfer pricing or from changes in the rules governing transfer pricing, the repatriation of non-U.S. earnings for which we have not previously provided for U.S. taxes, the availability of the U.S. research and development tax credit, and other changes in tax laws and regulations. We cannot give any assurance as to what our effective tax rate will be in the future because, among other things, there is uncertainty regarding the tax policies of the jurisdictions where we operate. Changes in tax laws, such as tax reform in the United States or changes in tax laws resulting from the Organization for Economic Co-operation and Development's multi-jurisdictional plan of action to address base erosion and profit shifting, could impact our effective tax rate. Any significant increase in our future effective tax rate could reduce net income for future periods and may have a material adverse impact on our results of our operations.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our or our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts, and business operations or environmental damage that could result in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages—and such liability could exceed our resources—and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

***Risks generally associated with a company-wide implementation of an enterprise resource planning (ERP) system may adversely affect our business and results of operations or the effectiveness of our internal controls over financial reporting.***

We are in the process of implementing a company-wide ERP system to upgrade certain existing business, operational, and financial processes. Our ERP implementation is a complex and time-consuming project that we expect will require more than a year to complete. Our results of operations could be adversely affected if we experience time delays or cost overruns during the ERP implementation process, or if the ERP system or associated process changes do not give rise to the benefits that we expect. This project has required and may continue to require investment of capital and human resources, the re-engineering of processes of our business, including our procurement process, and the attention of many employees who would otherwise be focused on other aspects of our business. Any deficiencies in the design and implementation of the new ERP system could result in potentially much higher costs than we had incurred and could adversely affect our ability to develop and launch solutions, provide services, fulfill contractual obligations, file reports with the SEC in a timely manner, operate our business or otherwise affect our controls environment. Any of these consequences could have an adverse effect on our results of operations and financial condition.

***Our business and operations may be materially adversely affected in the event of computer system failures or security breaches.***

Despite the implementation of security measures, our internal computer systems, and those of our contract research organizations and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyber-attacks, natural disasters, fire, terrorism, war and telecommunication and electrical failures. If such an event were to occur and interrupt our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, including protected health information, we could incur liability and the further development of our drug candidates could be delayed. We may also be vulnerable to cyber-attacks by hackers or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business or result in legal proceedings.

***We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Our corporate headquarters and laboratory are located in the San Francisco Bay Area, and our collaboration partner for KRN23, KHK, is located in Japan, which have both in the past experienced severe earthquakes and other natural disasters. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations or those of our collaborators, and have a material adverse effect on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage, or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure (such as the manufacturing facilities of our third-party contract manufacturers) or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

***Risks Related to Ownership of Our Common Stock***

***The market price of our common stock may be highly volatile.***

The market price of our common stock has been, and is likely to continue to be, volatile, including for reasons unrelated to changes in our business. Our stock price could be subject to wide fluctuations in response to a variety of factors, including but not limited to the following:

- adverse results or delays in preclinical or clinical studies;
- any inability to obtain additional funding;
- any delay in filing an IND, NDA, BLA, MAA, or other regulatory submission for any of our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory agency's review of that IND, NDA, BLA, MAA, or other regulatory submission;
- the perception of limited market sizes or pricing for our product candidates;
- failure to successfully develop and commercialize our product candidates;
- the level of any revenue we receive from named patient sales;
- post-marketing safety issues;
- failure to maintain our existing strategic collaborations or enter into new collaborations;

- failure by us or our licensors and strategic collaboration partners to prosecute, maintain, or enforce our intellectual property rights;
- changes in laws or regulations applicable to our products;
- any inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the financial projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partner, or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- securities or industry analysts' reports regarding our stock, or their failure to issue such reports;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

***Our principal stockholders and management own a significant percentage of our stock and may be able to exert significant control over matters subject to stockholder approval.***

As of February 19, 2016, our executive officers, directors, greater than five percent stockholders, and their affiliates beneficially owned approximately 57% of our voting stock. Therefore, these stockholders may have the ability to influence us through their ownership positions, which may prevent or discourage unsolicited acquisition proposals or offers for our common stock that certain other stockholders may believe are in their best interests.

***Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.***

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities, or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2014 Incentive Plan, or the 2014 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors, and consultants. An aggregate of 2,250,000 shares were available for issuance at the inception of the 2014 Plan. The number of shares available for future grant under the 2014 Plan will automatically increase on January 1 of each year (as of January 1, 2015) by the lesser of 2,500,000 shares or 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2014 Plan each year.

Pursuant to our 2014 Employee Stock Purchase Plan, or 2014 ESPP, eligible employees can acquire shares of our common stock at a discount to the prevailing market price, and an aggregate of 600,000 shares were available for issuance at the inception of the 2014 ESPP. The number of shares available for issuance under the 2014 ESPP will automatically increase on January 1 of each year (as of January 1, 2015) by the lesser of 1,200,000 shares or 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year. If our board of directors elects to increase the number of shares available for future grant under the 2014 Plan or the 2014 ESPP, our stockholders may experience additional dilution, which could cause our stock price to fall.

***Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.***

We have incurred substantial losses during our history and do not expect to become profitable in the near future nor may we ever achieve profitability. To the extent that we continue to generate taxable losses, unused taxable losses will, subject to certain limitations, carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an “ownership change,” generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards, or NOL carryforwards, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. An analysis to determine limitations upon our NOL carryforwards and other pre-change tax attributes for ownership changes that have occurred previously has been performed, resulting in a permanent decrease of NOL carryforwards in the amount of \$6.9 million and a permanent decrease in research tax credit carryforwards in the amount of \$0.3 million. As a result of these decreases and others that may occur as a result of future ownership changes, our ability to use our pre-change NOL carryforwards and other tax attribute carryforwards to offset U.S. federal taxable income and tax liabilities is limited and may become subject to even greater limitations, which could potentially accelerate or permanently increase future federal tax liabilities for us. In addition, there may be periods during which the use of state income tax NOL carryforwards and other state tax attribute carryforwards (such as state research tax credits) are suspended or otherwise limited, which could potentially accelerate or permanently increase future state tax liabilities for us.

***We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.***

We have never declared or paid any 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 connection with our initial public offering, or IPO, in February 2014, all dividends paid 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, for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

***Provisions in our amended and restated certificate of incorporation and by-laws, as well as provisions of Delaware law, could make it more difficult for a third-party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.***

Our amended and restated certificate of incorporation, amended and restated by-laws, and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and by-laws include provisions that:

- authorize “blank check” preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend, and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors or the chairperson of our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated by-laws; and
- require holders of 75% of our outstanding common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay, deter, or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our amended and restated certificate of incorporation or amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

**Item 1B. *Unresolved Staff Comments***

None.

**Item 2. *Properties***

Our primary operations are conducted at the leased facilities described below.

We lease approximately 108,000 square feet of office space in Novato, California used primarily for corporate, clinical, regulatory, manufacturing, quality, and commercial functions. The lease for approximately 83,000 of the 108,000 square feet will expire on April 30, 2019 and the lease for approximately 25,000 of the 108,000 square feet will expire on December 31, 2020.

We also lease a 5,983 square foot facility in Novato, California used for research laboratory space. The rental term for this space will expire on September 15, 2019.

We also lease approximately 63,000 square feet of office space in Brisbane, California. The term of the lease will commence no later than May 1, 2016, and it expires on June 30, 2026.

We believe our facilities are adequate and suitable for our current needs, and that we will be able to obtain new or additional leased space in the future when necessary.

**Item 3. *Legal Proceedings***

We are not currently a party to any material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties and we may, from time to time, make claims or take legal actions to assert our rights, including intellectual property rights as well as claims relating to employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our consolidated operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

**Item 4. *Mine Safety Disclosures***

Not applicable.

**PART II**

**Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities**

Our common stock has been traded on The NASDAQ Global Select Market since January 31, 2014 under the symbol "RARE". Prior to such time, there was no public market for our common stock. As a result, we have not set forth quarterly information with respect to the high and low prices for our common stock for the two most recent fiscal years. The following tables set forth the intraday high and low prices of our common stock as reported by NASDAQ from January 31, 2014, our first day of trading on NASDAQ, to December 31, 2015. On February 19, 2016, the closing price of our common stock on the NASDAQ Global Select Market was \$63.27 per share.

	<b>Fiscal 2014</b>	
	<b>High</b>	<b>Low</b>
First Quarter (January 31, 2014 through March 31, 2014)	\$ 69.77	\$ 35.15
Second Quarter	\$ 60.00	\$ 32.02
Third Quarter	\$ 60.04	\$ 37.77
Fourth Quarter	\$ 58.33	\$ 38.01

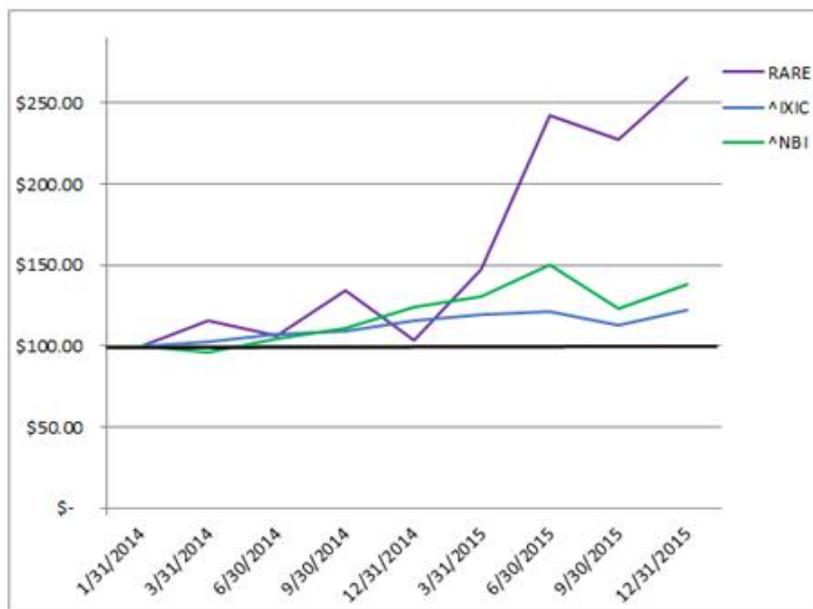
  

	<b>Fiscal 2015</b>	
	<b>High</b>	<b>Low</b>
First Quarter	\$ 65.35	\$ 44.27
Second Quarter	\$ 105.97	\$ 56.11
Third Quarter	\$ 137.05	\$ 83.40
Fourth Quarter	\$ 117.12	\$ 79.34

As of February 19, 2016, we had 3 holders of record of our common stock. Certain shares are held in "street" name and, accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number.

## STOCK PRICE PERFORMANCE GRAPH

The following stock performance graph compares our total stock return with the total return for (i) the NASDAQ Composite Index and the (ii) the NASDAQ Biotechnology Index for the period from January 31, 2014 (the date our common stock commenced trading on the NASDAQ Global Market) through December 31, 2015. The figures represented below assume an investment of \$100 in our common stock at the closing price of \$42.25 on January 31, 2014 and in the NASDAQ Composite Index and the NASDAQ Biotechnology Index on January 31, 2014 and the reinvestment of dividends into shares of common stock. The comparisons in the table are required by the Securities and Exchange Commission, or SEC, and are not intended to forecast or be indicative of possible future performance of our common stock. This graph shall not be deemed “soliciting material” or be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



\$100 investment in stock or index	Ticker	January 31, 2014	December 31, 2014	December 31, 2015
Ultragenyx Pharmaceutical Inc.	RARE	\$ 100.00	\$ 103.86	\$ 265.51
NASDAQ Composite Index	^IXIC	\$ 100.00	\$ 115.40	\$ 122.02
NASDAQ Biotechnology Index	^NBI	\$ 100.00	\$ 123.70	\$ 137.83

### Dividend Policy

We have never declared or paid cash dividends on our common stock. Although we paid dividends to our holders of preferred stock in the past, including a \$4.3 million cash dividend paid in connection with our IPO in February 2014, all dividends paid 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, operation, 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.

### Information About Our Equity Compensation Plans

Information regarding our equity compensation plans is incorporated by reference to Item 12, “Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters—Equity Compensation Plan Information” of Part III of this Annual Report on Form 10-K.

### Issuer’s Purchases of Equity Securities

None

**Item 6. Selected Consolidated Financial Data**

The information set forth below for the five years ended December 31, 2015 is not necessarily indicative of the results that may be expected in the future and interim results are not necessarily indicative of results to be expected for the full year. You should read the selected historical financial data below in conjunction with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

	Year Ended December 31,				
	2015	2014	2013	2012	2011
	(in thousands, except share and per share amounts)				
<b>Consolidated Statements of Operations Data:</b>					
Operating expenses:					
Research and development	\$ 114,737	\$ 45,967	\$ 27,829	\$ 12,641	\$ 4,717
General and administrative	33,001	10,811	4,451	3,344	1,844
Total operating expenses	<u>147,738</u>	<u>56,778</u>	<u>32,280</u>	<u>15,985</u>	<u>6,561</u>
Loss from operations	(147,738)	(56,778)	(32,280)	(15,985)	(6,561)
Interest income	2,320	608	216	1	4
Interest expense	—	—	—	—	(270)
Other expense	(200)	(3,632)	(3,006)	(350)	(22)
Net loss	<u>\$ (145,618)</u>	<u>\$ (59,802)</u>	<u>\$ (35,070)</u>	<u>\$ (16,334)</u>	<u>\$ (6,849)</u>
Net loss attributable to common stockholders <sup>(1)</sup>	<u>\$ (145,618)</u>	<u>\$ (64,610)</u>	<u>\$ (50,289)</u>	<u>\$ (19,561)</u>	<u>\$ (7,466)</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (3.96)</u>	<u>\$ (2.25)</u>	<u>\$ (14.87)</u>	<u>\$ (14.20)</u>	<u>\$ (4.62)</u>
Shares used to compute net loss per share attributable to common stockholders, basic and diluted	<u>36,782,603</u>	<u>28,755,758</u>	<u>3,382,489</u>	<u>1,377,207</u>	<u>1,617,384</u>

(1) See Notes 2 and 12 to our audited consolidated financial statements of this report for an explanation of the calculations of basic and diluted net loss per share attributable to common stockholders.

	As of December 31,				
	2015	2014	2013	2012	2011
	(in thousands)				
<b>Consolidated Balance Sheets Data:</b>					
Cash, cash equivalents and investments	\$ 536,256	\$ 187,487	\$ 53,377	\$ 86,190	\$ 10,645
Working capital	422,289	180,899	49,304	83,257	9,954
Total assets	559,569	197,967	59,649	88,316	12,129
Convertible preferred stock warrant liability	—	—	3,419	518	216
Convertible preferred stock	—	—	124,930	111,387	18,604
Total stockholders' equity (deficit)	531,090	184,945	(74,821)	(27,047)	(7,961)

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this annual report entitled "Selected Financial Data" and our consolidated financial statements and related notes included elsewhere in this annual report. This discussion and other parts of this annual report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations, and intentions. In this annual report, words such as "may," "will," "expect," "anticipate," "estimate," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements, as described elsewhere herein. As a result of many factors, including those factors set forth in the "Risk Factors" section of this annual report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

### 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 target diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no currently 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 clinical-stage 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 in clinical development for the treatment of three diseases:

- KRN23, or UX023, is an antibody targeting fibroblast growth factor 23, or FGF23, in development for the treatment of 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 and a Phase 3 adult study in December 2015.
- KRN23 is also being developed for the treatment of TIO. TIO results from typically benign tumors that produce excess levels of FGF23, which can lead to severe hypophosphatemia, osteomalacia, fractures, fatigue, bone and muscle pain, and muscle weakness. We initiated a Phase 2 study of KRN23 in adult inoperable TIO patients in March 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-organ dysfunction, pervasive skeletal disease, and death. We completed enrollment of a Phase 3 clinical study in June 2015.

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

- UX007 is a synthetic triglyceride with a specifically designed chemical composition being studied in an open-label Phase 2 study for the treatment of LC-FAOD from which interim results were recently reported. LC-FAOD is a set of rare metabolic diseases that prevent the conversion of fat into energy and can cause low blood sugar, muscle rupture, and heart and liver disease. The company is planning for a Phase 3 study that it expects to initiate in 2017 after discussions with regulatory authorities. UX007 is also in a Phase 2 study for the treatment of Glut1 DS, a rare metabolic disease of brain energy deficiency that is characterized by seizures, developmental delay, and movement disorder. The Phase 2 study in Glut1 DS patients with seizures continues to enroll patients. A Phase 3 study in the movement disorder phenotype of Glut1 DS is expected to begin in the second half of 2016.
- Ace-ER, or UX001, is an extended-release form of aceneuramic acid in a Phase 2 extension study for the treatment of GNE myopathy, a neuromuscular disorder that causes muscle weakness and wasting. We initiated a Phase 3 study in May 2015 and filed a Marketing Authorization Application, or MAA, seeking conditional approval from the European Medicines Agency, or EMA, for the use of Ace-ER in the treatment of GNE myopathy which was accepted in October 2015.

## **Financial Operations Overview**

We are considered a clinical-stage company and have only a limited operating history. To date, we have invested substantially all of our efforts and financial resources to identifying, acquiring, and developing our product candidates, including conducting clinical studies and providing general and administrative support for these operations. To date, we have funded our operations primarily from the sale of equity securities.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were \$145.6 million, \$59.8 million and \$35.1 million for the years ended December 31, 2015, 2014 and 2013. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

## **Revenue**

To date, we have not generated any revenue. We do not expect to recognize any significant revenue until we obtain regulatory approval for any product candidates that we develop and commercialize our products or enter into collaborative agreements with third parties.

## **Research and Development Expenses**

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- expenses incurred under agreements with clinical study sites that conduct research and development activities on our behalf;
- expenses incurred under license agreements with third parties;
- employee and consultant-related expenses, which include salaries, benefits, travel, and stock-based compensation;
- laboratory and vendor expenses related to the execution of preclinical, non-clinical, and clinical studies;
- the cost of acquiring, developing, and manufacturing clinical study materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supply costs.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and clinical sites. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and the services are performed.

The largest component of our total operating expenses has historically been our investment in research and development activities, including the clinical development of our product candidates. We allocate research and development salaries, benefits, stock-based compensation, and indirect costs to our product candidates on a program-specific basis, and we include these costs in the program-specific expenses. We expect our research and development expenses will increase in absolute dollars in future periods as we continue to invest in research and development activities related to developing our product candidates, and as programs advance into later stages of development and we enter into larger clinical studies. The process of conducting the necessary clinical research to obtain FDA approval is costly and time consuming and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent, if any, we will generate revenue from the commercialization and sale of any of our product candidates.

## **General and Administrative Expenses**

General and administrative expenses consist primarily of personnel costs, allocated facilities costs, and other expenses for outside professional services, including legal, human resources, audit, and accounting services. Personnel costs consist of salaries, benefits, and stock-based compensation. We expect that our general and administrative expenses will increase in the future to support continued research and development activities, preparation for potential commercialization of our product candidates, and as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, or SEC, and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities, and other administration and professional services.

## **Interest income**

Interest income consists of interest earned on our cash, cash equivalents, and investments.

### **Other expense**

Other expense primarily consists of gains and losses resulting from the remeasurement of our convertible preferred stock warrant liability. We continued to record adjustments to the estimated fair value of the convertible preferred stock warrants until their conversion into warrants to purchase shares of our common stock at the completion of our initial public offering. At that time, we reclassified the convertible preferred stock warrant liability as additional paid-in capital, and we will no longer record any related periodic fair value adjustments.

### **Critical Accounting Policies and Significant Judgments and Estimates**

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. There have been no significant and material changes in our critical accounting policies in 2015, as compared to those disclosed in "Management's Discussion and Analysis of Financial Condition and Results of Operations-Critical Accounting Policies and Significant Judgments and Estimates" in our in our most recent Annual Report on Form 10-K filed with the SEC.

### **Accrued Research and Development, and Research and Development Expenses**

As part of the process of preparing consolidated financial statements, we are required to estimate and accrue expenses, the largest of which is related to accrued research and development expenses. This process involves reviewing contracts and purchase orders, identifying services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual costs.

We record accruals for estimated costs of research, preclinical and clinical studies, and manufacturing development. These costs are a significant component of our research and development expenses. A substantial portion of our ongoing research and development activities is conducted by third-party service providers. We accrue the costs incurred under our agreements with these third parties based on actual work completed in accordance with agreements established with these third parties. We determine the actual costs through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrual balance in each reporting period. As actual costs become known, we adjust our accruals. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. Our accrual is dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party vendors.

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation, lab supplies, materials and facility costs, as well as fees paid to other nonemployees and entities that conduct certain research and development activities on our behalf. Amounts incurred in connection with collaboration and license agreements are also included in research and development expense. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

To date, there have been no material differences from our accrued estimated expenses to the actual clinical trial expenses; however, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies and other research activities.

### **Stock-Based Compensation**

Stock-based compensation costs related to stock options granted to employees are measured at the date of grant based on the estimated fair value of the award, net of estimated forfeitures. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. We expect to continue to grant stock options in the future, and to the extent that we do, our actual stock-based compensation will likely increase. The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the estimated fair value of stock-based awards. These assumptions include:

- *Expected term* — The expected term represents the period that the stock-based awards are expected to be outstanding and is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term).

- *Expected volatility* — Prior to our IPO we were privately held and did not have any trading history for our common stock; accordingly, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which we based our expected stock price volatility, we selected companies with comparable characteristics to us, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. In 2014, we modified our approach by phasing in our own common stock trading history and supplemented the remaining historical information with a blended volatility from the trading history from the common stock of the same set of comparable publicly traded biopharmaceutical companies. We will continue to use comparable company information until historical volatility of our common stock is relevant to measure expected volatility for future option grants.
- *Risk-free interest rate* — The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.
- *Expected dividend* — We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

In addition to the assumptions used in the Black-Scholes option-pricing model, we must also estimate a forfeiture rate to calculate the stock-based compensation for our awards. We will continue to use judgment in evaluating the expected volatility, expected terms, and forfeiture rates utilized for our stock-based compensation calculations on a prospective basis and will revise in subsequent periods, if actual forfeitures differ from those estimates.

For the years ended December 31, 2015, 2014 and 2013 stock-based compensation expense was \$24.9 million, \$5.4 million and \$0.7 million, respectively. As of December 31, 2015, we had \$102.8 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 3.25 years.

#### *Fair Value of Common Stock*

We are required to estimate the fair value of the common stock underlying our stock-based awards when performing the fair value calculations with the Black-Scholes option-pricing model. Prior to our IPO in January 2014, the estimated fair value of the common stock underlying our stock-based awards was determined on each grant date by our board of directors, with input from management. Given the absence of a public trading market of our common stock, and in accordance with the American Institute of Certified Public Accountants, or AICPA, Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, our board of directors exercised reasonable judgment and considered numerous objective and subjective factors to estimate the fair value of our common stock.

All options to purchase shares of our common stock have been granted with an exercise price per share equal to the fair value per share of our common stock underlying those options on the date of grant. To assist our board of directors with the determination of the exercise price of our stock options and the fair value of the common stock underlying the options, we obtained third-party valuations of our common stock as of June 30, 2013, September 30, 2013, and November 30, 2013. Our board of directors considered the fair values of the common stock derived in the third-party valuations as one of the factors it considered when setting the exercise prices for options granted. Our board of directors also considered a range of objective and subjective factors and assumptions in estimating the fair value of our common stock on the date of grant, including:

- progress of our research and development efforts;
- our operating results and financial condition, including our levels of available capital resources;
- rights and preferences of our common stock compared to the rights and preferences of our other outstanding equity securities;
- our stage of development and material risks related to our business;
- the achievement of enterprise milestones, including entering into collaboration or license agreements and our progress in clinical trials;
- the valuation of publicly-traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- equity market conditions affecting comparable public companies;
- the likelihood of achieving a liquidity event for the shares of common stock, such as an initial public offering given prevailing market and biotechnology sector conditions; and
- that the grants involved illiquid securities in a private company.

The fair value of the underlying common stock was determined by the board of directors until the IPO when our common stock started trading on The NASDAQ Global Select Market under the ticker symbol RARE on January 31, 2014. Consequently, after our IPO the fair value of the shares of common stock underlying the stock options is the closing market price on the option grant date.

## Income Taxes

We use the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. We assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

As of December 31, 2015, our total deferred tax assets were \$109.5 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating losses and tax credit carryforwards. Utilization of the net operating loss and tax credit carryforwards may be subject to an annual limitation due to historical or future ownership percentage change rules provided by the Internal Revenue Code of 1986, and similar state provisions. The annual limitation may result in the expiration of certain net operating loss and tax credit carryforwards before their utilization.

## Results of Operations

### Comparison of Years Ended December 31, 2015 and 2014

#### Research and Development Expenses (dollars in thousands)

	Year Ended December 31,		Dollar Change	% Change
	2015	2014		
Development candidate:				
KRN23 (XLH)	\$ 11,834	\$ 4,691	\$ 7,143	152%
KRN23 (TIO)	1,052	—	1,052	*
rhGUS	18,989	9,445	9,544	101%
UX007 (LC-FAOD)	11,807	8,739	3,068	35%
UX007 (Glut1 DS)	8,145	4,475	3,670	82%
Ace-ER	24,164	10,851	13,313	123%
Other research costs and preclinical costs	38,746	7,766	30,980	399%
Total research and development expenses	\$ 114,737	\$ 45,967	\$ 68,770	150%

Research and development expenses increased \$68.8 million for the twelve months ended December 31, 2015 compared to the same period in 2014. The increase in research and development expenses above is primarily due to:

- for KRN23 (XLH), an increase of \$7.1 million related to the continued development of our clinical program including the initiation of our Phase 3 adult study and other development and regulatory activities, net of KHK reimbursement;
- for KRN23 (TIO), an increase of \$1.1 million related to the initiation and development of our adult TIO study in 2015 and other development and regulatory activities, net of KHK reimbursement;
- for rhGUS, an increase of \$9.5 million related to an increase in manufacturing, quality, and clinical study related activities, including the enrollment of our Phase 3 study;
- for UX007 (LC-FAOD), an increase of \$3.1 million related to clinical manufacturing and the continued development of our clinical program and support of investigator-sponsored studies across multiple diseases;
- for UX007 (Glut1 DS), an increase of \$3.7 million related to the continued development of our clinical program, including patient identification efforts;
- for Ace-ER, an increase of \$13.3 million related to the increase in clinical, manufacturing, quality and regulatory activities for this program, including the initiation of our Phase 3 trial and efforts associated with the conditional MAA filing; and
- an increase of \$31.0 million in other research and development costs includes: \$10.0 million for the Arcturus upfront license fee that was expensed in the fourth quarter of 2015, an increase of \$3.9 million related to the continued development of our pre-clinical programs, and an increase of \$17.1 million in non-program specific support and overhead costs, including stock compensation expenses.

We expect our research and development expenses to increase in the future as we advance our product candidates through clinical development. The timing and amount of expenses incurred will depend largely upon the outcomes of current or future clinical studies for our product candidates as well as the related regulatory requirements, manufacturing costs and any costs associated with the advancement of our preclinical programs.

*General and Administrative Expenses (dollars in thousands)*

	Year Ended December 31,		Dollar Change	% Change
	2015	2014		
General and administrative	\$ 33,001	\$ 10,811	\$ 22,190	205%

General and administrative expenses increased \$22.2 million for the year ended December 31, 2015 compared to the same period in 2014. The increase in general and administrative expenses was primarily due to increases in commercial planning costs, professional services costs, stock-based compensation and personnel costs resulting from an increase in employees in support of our operations.

We expect general and administrative expenses to increase to support our organizational growth, the costs of being a public company, and the growth of our global commercial operations.

*Interest Income (dollars in thousands)*

	Year Ended December 31,		Dollar Change	% Change
	2015	2014		
Interest income	\$ 2,320	\$ 608	\$ 1,712	282%

Interest income increased \$1.7 million for the year ended December 31, 2015 compared to the same period in 2014, primarily due to funds invested from our underwritten public offerings in July 2015, February 2015 and July 2014.

*Other Expense, net (dollars in thousands)*

	Year Ended December 31,		Dollar Change	% Change
	2015	2014		
Other expense, net	\$ 200	\$ 3,632	\$ (3,432)	-94%

Other expense, net decreased \$3.4 million for the year ended December 31, 2015 compared to the same period in 2014. This was primarily related to the fair value remeasurement of the liability related to our convertible preferred stock warrants. There was no corresponding expense in 2015 as the preferred stock warrants were converted to common stock warrants upon the completion of the IPO and are no longer subject to remeasurement.

**Comparison of Years Ended December 31, 2014 and 2013**

*Research and Development Expenses (dollars in thousands)*

	Year Ended December 31,		Dollar Change	% Change
	2014	2013		
Development candidate:				
KRN23 (XLH)	\$ 4,691	\$ 821	\$ 3,870	471%
rhGUS	9,445	7,180	2,265	32%
UX007 (LC-FAOD)	8,739	5,792	2,947	51%
UX007 (Glut1 DS)	4,475	2,400	2,075	86%
Ace-ER	10,851	8,054	2,797	35%
Other research costs and preclinical costs	7,766	3,582	4,184	117%
Total research and development expenses	<u>\$ 45,967</u>	<u>\$ 27,829</u>	<u>\$ 18,138</u>	65%

Research and development expenses increased \$18.1 million for the twelve months ended December 31, 2014 compared to the same period in 2013. The increase in research and development expenses above is primarily due to:

- for KRN23 (XLH), an increase of \$3.9 million related to the development and initiation of our pediatric study (in July 2014) and other development expenses since the product candidate was in-licensed in August 2013;
- for rhGUS, an increase of \$2.3 million related to an increase in manufacturing and clinical study related activities;

- for UX007 (LC-FAOD), an increase of \$2.9 million related to the initiation of our clinical program in 2013, support of investigator-sponsored studies, and costs related to manufacturing, partially offset by the \$0.8 million we paid to exercise the option with Baylor Research Institute, or BRI, pursuant to our license agreement with BRI to license the rights to UX007 in all territories outside of North America in June 2013;
- for UX007 (Glut1 DS), an increase of \$2.1 million related to costs associated with the initiation of our clinical program and costs related to manufacturing;
- for Ace-ER, an increase of \$2.8 million related to the increase in clinical activities and related manufacturing for this program; and
- an increase of \$4.2 million in other research costs and preclinical costs for various other potential product candidates.

General and Administrative Expenses (dollars in thousands)

	Year Ended December 31,		Dollar Change	% Change
	2014	2013		
General and administrative	\$ 10,811	\$ 4,451	\$ 6,360	143%

General and administrative expenses increased \$6.4 million for the year ended December 31, 2014 compared to the same period in 2013. The increase in general and administrative expenses was primarily due to increases in professional services costs, costs associated with being a public company, and an increase in personnel costs as a result of increases in employee headcount.

Interest Income (dollars in thousands)

	Year Ended December 31,		Dollar Change	% Change
	2014	2013		
Interest income	\$ 608	\$ 216	\$ 392	181%

Interest income increased \$0.4 million for the year ended December 31, 2014 compared to the same period in 2013, primarily due to funds invested in 2014 from our IPO and underwritten public offering which were completed in January 2014 and July 2014, respectively.

Other Expense, net (dollars in thousands)

	Year Ended December 31,		Dollar Change	% Change
	2014	2013		
Other expense, net	\$ 3,632	\$ 3,006	\$ 626	21%

Other expense, net increased \$0.6 million for the year ended December 31, 2014 compared to the same period in 2013. This was primarily due to a \$0.4 million increase in expense for the fair value remeasurement of the liability related to our convertible preferred stock warrants combined with a \$0.3 million increase in state tax fees offset by \$0.1 million in foreign currency gains.

**Liquidity and Capital Resources**

Since our inception, we have funded our operations primarily with \$103.9 million in net proceeds from the sale of convertible preferred stock, \$121.7 million in net proceeds from the sale of common stock in our IPO and \$521.4 million in net proceeds from the sale of common stock in our underwritten public offerings. As of December 31, 2015, we had \$536.3 million in available cash, cash equivalents, and investments. Our cash, cash equivalents and investments are held in a variety of interest-bearing accounts, corporate debt securities, U.S government securities and money market accounts. Cash in excess of immediate requirements is invested with a view toward liquidity and capital preservation, and we seek to minimize the potential effects of concentration and credit risk.

The following table summarizes our cash flows for the periods indicated (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Cash used in operating activities	\$ (105,977)	\$ (44,634)	\$ (31,200)
Cash used in investing activities	(292,351)	(123,440)	(47,734)
Cash provided by financing activities	467,573	184,971	171
Net increase (decrease) in cash and cash equivalents	\$ 69,245	\$ 16,897	\$ (78,763)

### ***Cash Used in Operating Activities***

Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures. Due to our significant research and development expenditures, we have generated significant operating losses since our inception. Cash used to fund operating expenses is affected by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Cash used in operating activities for the year ended December 31, 2015 was \$106.0 million and reflected a net loss of \$145.6 million, offset by non-cash charges of \$1.4 million for depreciation and amortization, \$5.6 million for the amortization of premium paid on purchased investments, and \$24.9 million for stock-based compensation. Cash used in operating activities also reflected a \$7.1 million increase in prepaid expenses and other current assets primarily due to an increase in contract research organization, or CRO, prepaid clinical costs, an increase in KHK receivable and an increase in interest receivable, and a \$2.0 million decrease in accounts payable primarily due to the timing of payments. These increases were offset by a \$0.2 million decrease in non-current assets as result of a decrease in manufacturing prepaid expenses and a \$16.7 million increase in accrued expenses and other liabilities as a result of an increase in clinical study, manufacturing, related costs as we continued to increase our research and development activities and employee bonuses.

Cash used in operating activities for the year ended December 31, 2014 was \$44.6 million and reflected a net loss of \$59.8 million, offset by non-cash charges of \$0.7 million for depreciation and amortization, \$3.6 million for the amortization of premium paid on purchased short-term investments, \$5.4 million for stock-based compensation and \$3.3 million for the revaluation of convertible preferred stock warrant liability. Cash used in operating activities also reflected a \$4.1 million increase in prepaid expenses and other current assets primarily due to an increase in CRO prepaid expenses and an increase in interest income receivable as our invested funds increased with the closing of our IPO in February 2014 and our underwritten public offering in July 2014. Cash used in operations also reflected a \$0.4 million increase in long-term other assets primarily from the increase in CRO prepaid expenses and value added tax receivables. These increases were offset \$6.7 million increase in accounts payable and accrued liabilities primarily due to an increase in clinical study, manufacturing and related costs as we continued to increase our research and development activities.

Cash used in operating activities for the year ended December 31, 2013 was \$31.2 million and reflected a net loss of \$35.1 million, offset by non-cash charges of \$0.4 million for depreciation and amortization, \$1.4 million for the amortization of premium paid on purchased short-term investments, \$0.7 million for stock-based compensation and \$2.9 million for the revaluation of convertible preferred stock warrant liability. Cash used in operating activities also reflected a \$1.6 million increase in prepaid expenses and other current assets primarily due to an increase in CRO prepaid expenses and an increase in interest income receivable as our invested funds increased with the sale of our Series B convertible preferred stock in December 2012, and a \$2.6 million increase in other assets primarily related to deferred offering costs related to our IPO. These increases were offset by a \$2.7 million increase in accounts payable and accrued liabilities primarily due to higher clinical study and related costs as we continued to increase our research and development activities.

### ***Cash Used in Investing Activities***

Cash used in investing activities for the year ended December 31, 2015 was \$292.4 million and related to purchases of investments of \$624.2 million, purchases of property and equipment of \$5.0 million and an increase of \$1.5 million in restricted cash for the expansion of the space under our current lease, offset by proceeds from maturities of investments of \$249.0 million and the sale of investments of \$89.3 million.

Cash used in investing activities for the year ended December 31, 2014 was \$123.4 million and was related to purchases of short-term investments of \$209.0 million and property and equipment of \$2.1 million and an increase in restricted cash of \$0.3 million for the expansion of the space under our current lease, offset by proceeds from maturities of short-term investments of \$83.0 million, sales of investments of \$5.0 million.

Cash used in investing activities for the year ended December 31, 2013 was \$47.7 million and was related to purchases of short-term investments of \$64.0 million and property and equipment of \$0.4 million, offset by proceeds from maturities of short-term investments of \$16.6 million.

### ***Cash Flows Provided by Financing Activities***

Cash provided by financing activities for the year ended December 31, 2015 was \$467.6 million and was comprised of the net proceeds from the issuance of common stock from our underwritten public offerings and the exercise of stock options, restricted stock units, and warrants.

Cash provided by financing activities for the year ended December 31, 2014 was \$185.0 million and was comprised of \$189.3 million in proceeds from the issuance of common stock from our IPO and our underwritten public offering and proceeds from the exercise of stock options, offset by the payment of \$4.3 million dividend to our preferred stockholders in connection with the closing of our IPO.

Cash provided by financing activities for the year ended December 31, 2013 was \$0.2 million related to proceeds from the issuance of common stock for the exercise of stock options.

## Funding Requirements

We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We will likely require additional capital to fund our operations and complete our ongoing and planned clinical studies, and funding may not be available to us on acceptable terms or at all. We expect to satisfy future cash needs through existing capital balances or, if necessary, through equity or debt financings, or strategic collaborations. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may be required to delay, limit, reduce the scope of, or terminate one or more of our clinical studies, research and development programs or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our future funding requirements will depend on many factors, including the following:

- the scope, rate of progress, results and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing sales, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required upfront milestone and royalty payments thereunder.

We may seek to raise any necessary additional capital through some combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. To the extent that we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

## Contractual Obligations

We have contractual obligations from our operating leases, manufacturing and service contracts, licenses, royalties, development and collaboration arrangements, and other research and development activities. The following table summarizes our significant binding contractual obligations at December 31, 2015 (in thousands):

	Payments due by period				Total
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	
Operating leases	\$ 2,270	\$ 8,381	\$ 6,411	\$ 13,791	\$ 30,853
Manufacturing and service contracts	2,042	280	145	—	2,467
Total	\$ 4,312	\$ 8,661	\$ 6,556	\$ 13,791	\$ 33,320

## Newly Adopted Accounting Pronouncements

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements — Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, which requires management to evaluate, in connection with preparing financial statements for each annual and interim reporting period, whether there are conditions or events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued and provide related disclosures. This ASU will be effective for the Company in fiscal year 2016. Early adoption is permitted. We are currently assessing the future impact of this ASU on our financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes* (“ASU 2015-17”), which amends existing guidance to require that deferred income tax liabilities and assets be classified as noncurrent in a classified balance sheet, and eliminates the prior guidance which required an entity to separate deferred tax liabilities and assets into a current amount and a noncurrent amount in a classified balance sheet. The standard is effective for the Company in fiscal year 2017. Early adoption is permitted. As permitted by ASU 2015-17, the Company early-adopted this standard and applied it retrospectively to all periods of the tax provision presented. As the Company has full valuation allowance against the deferred assets, there is no impact to the financial statements. The Company has reflected the change of this pronouncement in Note 10 to the financial statements.

#### **Off-Balance Sheet Arrangements**

Since our inception in April 2010, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

#### **Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

Our exposure to market risk for changes in interest rates relates primarily to interest earned on our cash equivalents and investments. The primary objective of our investment activities is to preserve our capital to fund operations. A secondary objective is to maximize income from our investments without assuming significant risk. Our investment policy provides for investments in low-risk, investment-grade debt instruments. As of December 31, 2015, we had cash, cash equivalents and investments totaling \$536.3 million which includes bank deposits, money market funds, asset-backed securities, and investment-grade corporate bonds which are subject to default, changes in credit rating, and changes in market value. The securities in our investment portfolio are classified as available for sale and are subject to interest rate risk and will decrease in value if market interest rates increase. A hypothetical 10% change in interest rates during any of the periods presented would not have had a material impact on our financial statements. To date, we have not experienced a loss of principal on any of our investments.

We face foreign exchange risk as a result of entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. An adverse movement in foreign exchange rates could have a material effect on payments made to foreign suppliers and for license agreements. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our financial statements.

#### **Item 8. Financial Statements and Supplementary Data**

Our financial statements are annexed to this report beginning on page F-1 and are incorporated by reference into this Item 8.

#### **Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure**

None.

## **Item 9A. Controls and Procedures**

### **Evaluation of Disclosure Controls and Procedures**

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our “disclosure controls and procedures” as of the end of the period covered by this report, pursuant to Rules 13a-15(b) and 15d-15(b) under the Exchange Act of 1934, as amended, or the Exchange Act. In connection with that evaluation, our Chief Executive Officer and our Chief Financial Officer concluded that our disclosure controls and procedures were effective and designed to provide reasonable assurance that the information required to be disclosed is recorded, processed, summarized and reported within the time periods specified in the SEC rules and forms as of December 31, 2015. For the purpose of this review, disclosure controls and procedures means controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. These disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is accumulated and communicated to management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

### **Management’s Annual Report on Internal Control Over Financial Reporting**

Management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our management used the Committee of Sponsoring Organizations of the Treadway Commission Internal Control - Integrated Framework (2013), or the COSO framework, to evaluate the effectiveness of internal control over financial reporting. Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of our internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of our internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.

Management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2015 and has concluded that such internal control over financial reporting is effective.

Our independent registered public accounting firm, Ernst & Young LLP, has audited the financial statements included in this Annual Report on Form 10-K and has issued a report on the effectiveness of our internal control over financial reporting. The report of Ernst & Young LLP is included below.

### **Changes in Internal Control over Financial Reporting**

We are in the process of implementing a new enterprise resource planning, or ERP system, which will occur over a period of more than one year. During 2015, we completed the implementation of several significant ERP modules including core financial and purchasing modules. In connection with the implementation of the ERP system, we updated the processes that constitute our internal control over financial reporting, as necessary, to accommodate related changes to our business processes and accounting procedures. We will continue to implement additional ERP modules in a phased approach, including the implementation of supply chain modules which is currently in progress.

Certain processes that constitute our internal control over financial reporting have been materially affected by the implementation of several significant ERP modules and will require testing for effectiveness as the implementation progresses, we do not believe that the implementation of the ERP system has had or will have a material adverse effect on our internal control over financial reporting.

Except as otherwise described above, there have been no other changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during our fourth fiscal quarter ended December 31, 2015, that has materially affected, or is reasonably likely to materially affect our internal control over financial reporting.

## Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of  
Ultragenyx Pharmaceutical Inc.:

We have audited Ultragenyx Pharmaceutical Inc.'s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control–Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Ultragenyx Pharmaceutical Inc.'s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Ultragenyx Pharmaceutical Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the 2015 consolidated financial statements of Ultragenyx Pharmaceutical Inc. and our report dated February 25, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP  
Redwood City, California  
February 25, 2016

### Item 9B. Other Information

None.

## PART III

### **Item 10. Directors, Executive Officers and Corporate Governance**

Incorporated by reference from the information in our Proxy Statement for our 2016 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

We have adopted a Code of Ethics that applies to all of our directors, officers and employees, including our principal executive, principal financial and principal accounting officers, or persons performing similar functions. Our Code of Ethics is posted on our corporate governance website located at [www.ultragenyx.com](http://www.ultragenyx.com). We intend to disclose future amendments to certain provisions of the Code of Ethics, and waivers of the Code of Ethics granted to executive officers and directors, on the website within four business days following the date of the amendment or waiver.

### **Item 11. Executive Compensation**

Incorporated by reference from the information in our Proxy Statement for our 2016 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

### **Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

Incorporated by reference from the information in our Proxy Statement for our 2016 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

### **Item 13. Certain Relationships and Related Transactions and Director Independence**

Incorporated by reference from the information in our Proxy Statement for our 2016 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

### **Item 14. Principal Accountant Fees and Services**

Incorporated by reference from the information in our Proxy Statement for our 2016 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

**PART IV**

**Item 15. Exhibits and Financial Statement Schedules**

(a) The following documents are filed as part of this report.

(1) Consolidated Financial Statements

Consolidated Financial Statements—See Index to Consolidated Financial Statements at page F-1 of this report.

(2) Consolidated Financial Statement Schedules

Consolidated Financial statement schedules have been omitted in this report because they are not applicable, not required under the instructions, or the information requested is set forth in the consolidated financial statements or related notes thereto.

(b) Exhibits

The exhibits listed in the accompanying index to exhibits are incorporated by reference or filed as part of this report.



**Ultragenyx Pharmaceutical Inc.**  
**INDEX TO FINANCIAL STATEMENTS**

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## Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of  
Ultragenyx Pharmaceutical Inc.:

We have audited the accompanying consolidated balance sheets of Ultragenyx Pharmaceutical Inc. as of December 31, 2015 and 2014, and the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of the Ultragenyx Pharmaceutical Inc. at December 31, 2015 and 2014, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Ultragenyx Pharmaceutical Inc.'s internal control over financial reporting as of December 31, 2015, based on criteria established in *Internal Control-Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 25, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP  
Redwood City, California  
February 25, 2016

**ULTRAGENYX PHARMACEUTICAL INC.**  
**CONSOLIDATED BALANCE SHEETS**  
(In thousands, except share and per share amounts)

	<b>December 31,</b>	
	<b>2015</b>	<b>2014</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 93,569	\$ 24,324
Short-term investments	343,428	163,163
Restricted cash	150	—
Prepaid expenses and other current assets	13,060	5,929
<b>Total current assets</b>	<b>450,207</b>	<b>193,416</b>
Property and equipment, net	7,373	3,033
Restricted cash	2,135	744
Long-term investments	99,259	—
Other assets	595	774
<b>Total assets</b>	<b>\$ 559,569</b>	<b>\$ 197,967</b>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 2,942	\$ 4,857
Accrued liabilities	24,784	7,575
Deferred rent—current portion	192	85
<b>Total current liabilities</b>	<b>27,918</b>	<b>12,517</b>
Other liabilities	561	505
<b>Total liabilities</b>	<b>28,479</b>	<b>13,022</b>
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, par value of \$0.001 per share—25,000,000 shares authorized; nil outstanding as of December 31, 2015 and 2014	—	—
Common stock, par value of \$0.001 per share—250,000,000 shares authorized; 38,882,394 and 31,934,682 shares issued and outstanding as of December 31, 2015 and 2014	39	32
Additional paid-in capital	816,578	324,128
Accumulated other comprehensive loss	(868)	(174)
Accumulated deficit	(284,659)	(139,041)
<b>Total stockholders' equity</b>	<b>531,090</b>	<b>184,945</b>
<b>Total liabilities and stockholders' equity</b>	<b>\$ 559,569</b>	<b>\$ 197,967</b>

See accompanying notes.

**ULTRAGENYX PHARMACEUTICAL INC.**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**  
(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2015	2014	2013
Operating expenses:			
Research and development	\$ 114,737	\$ 45,967	\$ 27,829
General and administrative	33,001	10,811	4,451
Total operating expenses	<u>147,738</u>	<u>56,778</u>	<u>32,280</u>
Loss from operations	(147,738)	(56,778)	(32,280)
Other income (expense), net:			
Interest income	2,320	608	216
Other expense, net	(200)	(3,632)	(3,006)
Total other income (expense), net	<u>2,120</u>	<u>(3,024)</u>	<u>(2,790)</u>
Net loss	<u>\$ (145,618)</u>	<u>\$ (59,802)</u>	<u>\$ (35,070)</u>
Net loss attributable to common stockholders	<u>\$ (145,618)</u>	<u>\$ (64,610)</u>	<u>\$ (50,289)</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (3.96)</u>	<u>\$ (2.25)</u>	<u>\$ (14.87)</u>
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	<u>36,782,603</u>	<u>28,755,758</u>	<u>3,382,489</u>

See accompanying notes.

**ULTRAGENYX PHARMACEUTICAL INC.**  
**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**  
**(In thousands)**

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
Net loss	\$ (145,618)	\$ (59,802)	\$ (35,070)
Other comprehensive income (loss):			
Unrealized gain (loss) on available-for-sale securities	(694)	(185)	11
Total comprehensive loss	<u>\$ (146,312)</u>	<u>\$ (59,987)</u>	<u>\$ (35,059)</u>

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)  
(In thousands, except share and per share amounts)

	Convertible Preferred Stock				Stockholders' Equity (Deficit)					
	Series A Redeemable Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance as of December 31, 2012	34,349,894	\$ 37,458	27,081,680	\$ 73,929	3,458,928	\$ 3	\$ 8	\$ —	\$ (27,058)	\$ (27,047)
Issuance of common stock upon exercise of stock options	—	—	—	—	307,361	1	170	—	—	171
Employee stock-based compensation	—	—	—	—	—	—	389	—	—	389
Stock-based compensation expense related to founder's stock	—	—	—	—	—	—	268	—	—	268
Accretion on convertible preferred stock	—	13,543	—	—	—	—	(835)	—	(12,708)	(13,543)
Unrealized gain on available-for-sale securities	—	—	—	—	—	—	—	11	—	11
Net loss	—	—	—	—	—	—	—	—	(35,070)	(35,070)
Balance as of December 31, 2013	34,349,894	51,001	27,081,680	73,929	3,766,289	4	—	11	(74,836)	(74,821)
Accretion on convertible preferred stock	—	4,430	—	—	—	—	(27)	—	(4,403)	(4,430)
Conversion of convertible preferred stock to common stock	(34,349,894)	(55,431)	(27,081,680)	(73,929)	19,598,486	19	129,341	—	—	129,360
Reclassification of preferred stock warrant liability	—	—	—	—	—	—	6,743	—	—	6,743
Issuance of common stock in connection with initial public offering, net of issuance costs and preferred stock dividend	—	—	—	—	6,624,423	7	121,704	—	—	121,711
Issuance of common stock in connection with underwritten public offering, net of issuance costs	—	—	—	—	1,613,879	2	60,237	—	—	60,239
Employee stock-based compensation	—	—	—	—	—	—	5,394	—	—	5,394
Issuance of common stock upon exercise of stock options and warrants	—	—	—	—	331,605	—	736	—	—	736
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	(185)	—	(185)
Net loss	—	—	—	—	—	—	—	—	(59,802)	(59,802)
Balance as of December 31, 2014	—	—	—	—	31,934,682	32	324,128	(174)	(139,041)	184,945
Issuance of common stock in connection with underwritten public offering, net of issuance costs	—	—	—	—	5,980,000	6	461,130	—	—	461,136
Employee stock-based compensation	—	—	—	—	—	—	24,884	—	—	24,884
Issuance of common stock upon exercise of stock options and warrants	—	—	—	—	957,587	1	7,354	—	—	7,355
Restricted stock units vested during the period, net	—	—	—	—	10,125	—	(918)	—	—	(918)
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	(694)	—	(694)
Net loss	—	—	—	—	—	—	—	—	(145,618)	(145,618)
Balance as of December 31, 2015	—	\$ —	—	\$ —	38,882,394	\$ 39	\$ 816,578	\$ (868)	\$ (284,659)	\$ 531,090

See accompanying notes.

**ULTRAGENYX PHARMACEUTICAL INC.**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(In thousands)

	Year Ended December 31,		
	2015	2014	2013
<b>Operating activities:</b>			
Net loss	\$ (145,618)	\$ (59,802)	\$ (35,070)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,384	684	444
Amortization of premium on investment securities	5,637	3,600	1,413
Stock-based compensation	24,884	5,394	657
Revaluation of convertible preferred stock warrant liability	—	3,324	2,901
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(7,131)	(4,081)	(1,593)
Other assets	179	(411)	(2,615)
Accounts payable	(1,982)	3,177	237
Accrued expenses and other liabilities	16,670	3,481	2,426
Net cash used in operating activities	<u>(105,977)</u>	<u>(44,634)</u>	<u>(31,200)</u>
<b>Investing activities:</b>			
Purchase of property and equipment	(4,955)	(2,149)	(407)
Purchase of investments	(624,226)	(208,972)	(63,953)
Proceeds from sale of investments	89,321	5,002	—
Proceeds from maturities of investments	249,050	82,972	16,601
Decrease (increase) in restricted cash	(1,541)	(293)	25
Net cash used in investing activities	<u>(292,351)</u>	<u>(123,440)</u>	<u>(47,734)</u>
<b>Financing activities:</b>			
Proceeds from issuance of common stock, net	467,573	189,317	171
Payment of preferred stock dividend	—	(4,346)	—
Net cash provided by financing activities	<u>467,573</u>	<u>184,971</u>	<u>171</u>
Net increase (decrease) in cash and cash equivalents	69,245	16,897	(78,763)
Cash and cash equivalents at beginning of year	24,324	7,427	86,190
Cash and cash equivalents at end of year	<u>\$ 93,569</u>	<u>\$ 24,324</u>	<u>\$ 7,427</u>
<b>Supplemental disclosures of non-cash investing and financing information:</b>			
Costs of fixed assets included in accounts payable and accrued liabilities	<u>\$ 769</u>	<u>\$ 243</u>	<u>\$ —</u>
Reclassification of warrant liability to equity upon conversion to common stock warrants	<u>\$ —</u>	<u>\$ 6,743</u>	<u>\$ —</u>
Conversion of Series A and Series B preferred stock to common stock	<u>\$ —</u>	<u>\$ 129,360</u>	<u>\$ —</u>

See accompanying notes.

# ULTRAGENYX PHARMACEUTICAL INC.

## Notes to Consolidated Financial Statements

### 1. Organization and Basis of Presentation

Ultragenyx Pharmaceutical Inc. (the Company) is a biopharmaceutical company and was incorporated in California on April 22, 2010. The Company subsequently reincorporated in the state of Delaware in June 2011.

The Company is 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 metabolic genetic diseases. The Company is currently conducting a Phase 3 study of aceneuramic acid extended-release (Ace-ER) in patients with GNE myopathy (GNEM), which is also known as hereditary inclusion body myopathy (HIBM), a progressive muscle-wasting disorder; a Phase 3 study of recombinant human beta-glucuronidase (rhGUS) in patients with mucopolysaccharidosis 7, or MPS 7, a rare lysosomal storage disease; a Phase 2 clinical study for UX007 in patients with glucose transporter type-1 deficiency syndrome (Glut1 DS), a brain energy deficiency; a Phase 2 clinical study of UX007 in patients severely affected by long-chain fatty acid oxidation disorders (LC-FAOD), a genetic disorder in which the body is unable to convert long chain fatty acids into energy; and Phase 2 and Phase 3 studies of KRN23, an antibody targeting fibroblast growth factor 23, or FGF23, in patients with X-linked hypophosphatemia (XLH) and tumor-induced osteomalacia (TIO), both rare diseases that impair bone mineralization. The Company operates in the United States of America and has one reportable segment.

In the course of its research activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development activities. Management expects to incur additional losses in the future to conduct product research and development and recognizes the need to raise additional capital to fully implement its business plan. Through December 31, 2015, the Company has relied primarily on the proceeds from equity offerings to finance its operations.

On January 30, 2014, the Company's registration statements on Form S-1 (File Nos. 333-192244 and 333-193675) relating to its initial public offering (IPO) of its common stock were declared effective by the Securities and Exchange Commission (SEC). The shares began trading on The NASDAQ Global Select Market on January 31, 2014. The public offering price of the shares sold in the offering was \$21.00 per share. The IPO closed on February 5, 2014 and included 6,624,423 shares of common stock, which included 864,054 shares of common stock issued pursuant to the over-allotment option granted to the underwriters. The Company received total proceeds from the offering of \$129.4 million, net of underwriting discounts and commissions of \$9.7 million. After deducting offering expenses of approximately \$3.3 million and a cash dividend of \$4.3 million, which was paid to the preferred stockholders on the closing date, net proceeds were approximately \$121.7 million. Upon the closing of the IPO, all shares of convertible preferred stock then outstanding converted into 19,598,486 shares of common stock and the Series A convertible preferred stock warrants were converted into warrants to purchase common stock.

In July 2014, the Company completed an underwritten public offering in which the Company sold 1,613,879 shares of common stock, which included 302,602 shares of common stock purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of \$40.00 per share. In addition, certain existing stockholders sold 706,072 shares of common stock in the underwritten public offering at the same per-share price. The total proceeds that the Company received from the offering were approximately \$60.7 million, net of underwriting discounts and commissions of approximately \$3.9 million. After deducting estimated offering expenses payable of approximately \$0.4 million, net proceeds were \$60.2 million.

In February 2015, the Company completed an underwritten public offering in which the Company sold 3,450,000 shares of common stock, which included 450,000 shares of common stock purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of \$54.00 per share. The total proceeds that the Company received from the offering were approximately \$175.1 million, net of underwriting discounts and commissions of approximately \$11.2 million. After deducting offering expenses of \$0.6 million, net proceeds were \$174.5 million.

In July 2015, the Company completed an underwritten public offering in which the Company sold 2,530,000 shares of common stock, which included 330,000 shares of common stock purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of \$120.00 per share. The total proceeds that the Company received from the offering were approximately \$286.9 million, net of underwriting discounts and commissions of approximately \$16.7 million. After deducting offering expenses payable of approximately \$0.2 million, net proceeds were \$286.7 million.

The Company intends to raise additional capital through the issuance of equity, borrowings, or strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans.

### 2. Summary of Significant Accounting Policies

#### Basis of Consolidation

The consolidated financial statements include the accounts of Ultragenyx Pharmaceutical Inc. and our subsidiaries. All intercompany balances and transactions have been eliminated.

### **Use of Estimates**

The accompanying consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles (“GAAP”). The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent liabilities and the reported amounts of expenses in the consolidated financial statements and the accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to clinical trial accruals, fair value of assets and liabilities, warrants, common stock, income taxes and stock-based compensation. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

### **Cash and Cash Equivalents**

The Company considers all highly liquid investments with original maturities of three months or less from the date of purchase to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market accounts and corporate bonds.

### **Investments**

All investments have been classified as “available-for-sale” and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its investments in debt securities at the time of purchase and reevaluates such designation as of each balance sheet date. Investments with a maturity of one year or less from the balance sheet date are reported as short-term investments and investments with a maturity of greater than one year from the balance sheet date are reported as long-term investments. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest income and other expense, net, respectively. The cost of securities sold is based on the specific-identification method. Interest on investments is included in interest income.

### **Concentration of Credit Risk and Other Risks and Uncertainties**

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents, and investments. The Company’s cash, cash equivalents, and investments are held by financial institutions that management believes are of high credit quality. The Company’s investment policy limits investments to fixed income securities denominated and payable in U.S. dollars such as U.S. government obligations, money market instruments and funds, corporate bonds, and asset-backed securities and places restrictions on maturities and concentrations by type and issuer. Such deposits may, at times, exceed federally insured limits. The Company has not experienced any losses on its deposits of cash and cash equivalents and its accounts are monitored by management to mitigate risk. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents, corporate bond issuers and other financial instruments to the extent recorded in the balance sheets.

### **Property and Equipment**

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the respective assets. Depreciation and amortization begins at the time the asset is placed in service. Maintenance and repairs are charged to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss, if any, is reflected in operations.

The useful lives of the property and equipment are as follows:

Research and development equipment	5 years
Furniture and office equipment	5 years
Computer equipment	3 years
Software	3-5 years
Leasehold improvements	Shorter of lease term or estimated useful life

### **Impairment of Long-Lived Assets**

The Company evaluates its long-lived assets, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. Recoverability of these assets is measured by comparison of the carrying amount of each asset to the future undiscounted cash flows expected to result from the use of the asset and its eventual disposition. If the asset is considered to be impaired, the amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. The Company has not recorded impairment of any long-lived assets since inception.

### **Restricted Cash**

Restricted cash includes money market accounts with one of the Company's financial institutions as collateral for its obligations under its facility leases of the Company's corporate headquarters in Novato, California and for its facilities in Brisbane, California. Restricted cash also includes a savings account associated with a credit card agreement at one of the Company's financial institutions.

### **Accruals of Research and Development Costs**

The Company records accruals for estimated costs of research, preclinical and clinical studies and manufacturing development. These costs are a significant component of the Company's research and development expenses. A substantial portion of the Company's ongoing research and development activities are conducted by third-party service providers, including contract research organizations. The Company accrues the costs incurred under its agreements with these third parties based on actual work completed in accordance with agreements established with these third parties. The Company determines the actual costs through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. The Company makes significant judgments and estimates in determining the accrual balance in each reporting period. As actual costs become known, the Company adjusts its accruals. The Company has not experienced any material deviations between accrued clinical trial expenses and actual clinical trial expenses. However, actual services performed, number of patients enrolled, and the rate of patient enrollment may vary from the Company's estimates, resulting in adjustments to clinical trial expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations.

### **Leases**

The Company enters into lease agreements for its office and laboratory facilities. These leases are classified as operating leases. Rent expense is recognized on a straight-line basis over the term of the lease and, accordingly, the Company records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Incentives granted under the Company's facilities leases, including allowances to fund leasehold improvements, are deferred and are recognized as adjustments to rental expense on a straight-line basis over the term of the lease.

### **Comprehensive Loss**

Comprehensive loss is the change in stockholders' equity (deficit) from transactions and other events and circumstances other than those resulting from investments by stockholders and distributions to stockholders. The Company's other comprehensive loss is comprised of unrealized gains and losses on investments in available-for-sale securities.

### **Research and Development**

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation expense, lab supplies and facility costs, as well as fees paid to other nonemployees and entities that conduct certain research and development activities on the Company's behalf. Amounts incurred in connection with license agreements are also included in research and development expense. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

### **Stock-Based Compensation**

Stock-based awards issued to employees, including stock options, are recorded at fair value as of the grant date using the Black-Scholes option-pricing model and recognized as expense on a straight-line basis over the employee's requisite service period (generally the vesting period). Because noncash stock compensation expense is based on awards ultimately expected to vest, it is reduced by an estimate for future forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates.

### **Income Taxes**

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company must then assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. Due to the Company's lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits, as the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

### **Net Loss per Share Attributable to Common Stockholders**

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. The net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for the accretion on the Series A convertible preferred stock and cumulative dividends paid on Series A and B convertible preferred stock. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since the effects of potentially dilutive securities are antidilutive. In periods when we have incurred a net loss, convertible preferred stock, options and warrants to purchase common stock and convertible preferred stock warrants are considered common stock equivalents, but have been excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect is antidilutive.

### **Recent Accounting Pronouncements**

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements — Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, which requires management to evaluate, in connection with preparing financial statements for each annual and interim reporting period, whether there are conditions or events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued and provide related disclosures. This ASU will be effective for the Company in fiscal year 2016. Early adoption is permitted. The Company is currently assessing the future impact of this ASU in the financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"), which amends existing guidance to require that deferred income tax liabilities and assets be classified as noncurrent in a classified balance sheet, and eliminates the prior guidance which required an entity to separate deferred tax liabilities and assets into a current amount and a noncurrent amount in a classified balance sheet. The standard is effective for the Company in fiscal year 2017. Early adoption is permitted. As permitted by ASU 2015-17, the Company early-adopted this standard and applied it retrospectively to all periods of the tax provision presented. As the company has full valuation allowance against the deferred assets, there is no impact to the financial statements. The Company has reflected the change of this pronouncement in Note 10, Income Taxes.

### **3. Fair Value Measurements**

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

*Level 1*—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

*Level 2*—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

*Level 3*—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

The Company's financial instruments consist of Level 1 and Level 2 assets. Where quoted prices are available in an active market, securities are classified as Level 1. Money market funds are classified as Level 1. Level 2 assets consist primarily of corporate bonds, asset backed securities, commercial paper and U.S. Government agency securities based upon quoted market prices for similar movements in active markets, quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets. Where applicable these models project future cash flows and discount the future amounts to a present value using market-based observable inputs obtained from various third party data providers, including but not limited to, benchmark yields, interest rate curves, reported trades, broker/dealer quotes and reference data.

**ULTRAGENYX PHARMACEUTICAL INC.**  
**Notes to Consolidated Financial Statements (continued)**

The following table sets forth the fair value of the Company's financial assets and liabilities remeasured on a recurring basis based on the three-tier fair value hierarchy (in thousands):

	December 31, 2015			
	Level 1	Level 2	Level 3	Total
<b>Financial Assets:</b>				
Money market funds	\$ 53,254	\$ —	\$ —	\$ 53,254
Corporate bonds	—	370,445	—	370,445
Asset-backed securities	—	29,302	—	29,302
U.S. Government agency securities	—	47,452	—	47,452
Commercial paper	—	13,887	—	13,887
<b>Total financial assets</b>	<b>\$ 53,254</b>	<b>\$ 461,086</b>	<b>\$ —</b>	<b>\$ 514,340</b>

	December 31, 2014			
	Level 1	Level 2	Level 3	Total
<b>Financial Assets:</b>				
Money market funds	\$ 8,627	\$ —	\$ —	\$ 8,627
Corporate bonds	—	152,942	—	152,942
Asset-backed securities	—	9,542	—	9,542
U.S. Government agency securities	—	4,485	—	4,485
Other	—	209	—	209
<b>Total financial assets</b>	<b>\$ 8,627</b>	<b>\$ 167,178</b>	<b>\$ —</b>	<b>\$ 175,805</b>

**4. Balance Sheet Components**

**Cash Equivalents and Investments**

The fair values of cash equivalents, short-term investments, and long-term investments classified as available-for-sale securities, consisted of the following (in thousands):

	December 31, 2015			
	Amortized Cost	Gross Unrealized		Estimated Fair Value
		Gains	Losses	
Money market funds classified as cash equivalents	\$ 53,254	\$ —	\$ —	\$ 53,254
Corporate bonds classified as cash equivalents	18,403	—	(4)	18,399
Commercial Paper classified as short-term investments	13,887	—	—	13,887
Corporate bonds classified as short-term investments	282,386	9	(397)	281,998
Asset-backed securities classified as short-term investments	15,019	—	(27)	14,992
U.S Government agency securities classified as short-term investments	32,628	—	(77)	32,551
Corporate bonds classified as long-term investments	70,309	2	(263)	70,048
Asset-backed securities classified as long-term investments	14,337	—	(27)	14,310
U.S. Government agency securities classified as long-term investments	14,985	—	(84)	14,901
<b>Total</b>	<b>\$ 515,208</b>	<b>\$ 11</b>	<b>\$ (879)</b>	<b>\$ 514,340</b>

**ULTRAGENYX PHARMACEUTICAL INC.**  
**Notes to Consolidated Financial Statements (continued)**

	December 31, 2014			
	Amortized Cost	Gross Unrealized		Estimated Fair Value
		Gains	Losses	
Money market funds classified as cash equivalents	\$ 8,627	\$ —	\$ —	\$ 8,627
Corporate bonds classified as cash equivalents	3,806	1	—	3,807
Corporate bonds classified as short-term investments	149,303	4	(172)	149,135
Asset backed securities classified as short-term investments	9,546	—	(4)	9,542
U.S. Government agency securities classified as short-term investments	4,488	1	(4)	4,485
Other classified as cash equivalents	209	—	—	209
<b>Total</b>	<b>\$ 175,979</b>	<b>\$ 6</b>	<b>\$ (180)</b>	<b>\$ 175,805</b>

At December 31, 2015, the remaining contractual maturities of available-for-sale securities were less than three years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented.

**Property and Equipment, net**

Property and equipment, net consists of the following (in thousands):

	December 31,	
	2015	2014
Research and development equipment	\$ 1,302	\$ 712
Furniture and office equipment	944	572
Computer equipment	628	268
Software	1,622	821
Leasehold improvements	3,466	2,141
Construction-in-progress	2,276	—
Property and equipment, gross	10,238	4,514
Less accumulated depreciation	(2,865)	(1,481)
<b>Property and equipment, net</b>	<b>\$ 7,373</b>	<b>\$ 3,033</b>

Depreciation expense for the years ended December 31, 2015, 2014 and 2013 was \$1.4 million, \$0.7 million and \$0.4 million respectively. Amortization of leasehold improvements and software is included in depreciation expense.

**Accrued Liabilities**

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2015	2014
Research and clinical trial expenses	\$ 9,764	\$ 2,703
Payroll and related expenses	9,423	4,205
Consulting service expenses	4,193	122
Other	1,404	545
<b>Total accrued liabilities</b>	<b>\$ 24,784</b>	<b>\$ 7,575</b>

**5. License and Research Agreements**

**Nobelpharma License Agreement**

In September 2010, the Company entered into a collaboration and license agreement with Nobelpharma Co., Ltd. (Nobelpharma), which was amended in August 2015. Under the terms of this collaboration and license agreement, each party granted the other party a worldwide exclusive license under certain of that party's intellectual property related to the compound identified as N-acetylneuraminic acid, also known as sialic acid, to develop, manufacture, and commercialize products. Nobelpharma's licensed territory includes Japan and certain other Asian countries, and the Company's licensed territory includes the rest of the world.

The Company is required to make certain payments to Nobelpharma based upon achievement of certain development and approval milestones. The Company may make future payments that aggregate up to 200 million Yen (approximately \$1.7 million based on the exchange rate at December 31, 2015) that are contingent upon attainment of various development and approval milestones. The Company will pay a mid-single digit royalty on net sales in the Company's territory and will receive a mid-single digit royalty on net sales in the Nobelpharma territory, excluding Japan, if such product sales are ever achieved.

#### **Saint Louis University License Agreement**

In November 2010, the Company entered into a license agreement with Saint Louis University (SLU). Under the terms of this license agreement, SLU granted the Company an exclusive worldwide license to make, have made, use, import, offer for sale, and sell therapeutics related to SLU's beta-glucuronidase product for use in the treatment of human diseases.

The Company will be required to make a milestone payment of \$0.1 million upon approval of a glucuronidase-based enzyme therapy for treatment of MPS 7. Additionally, upon reaching a certain level of cumulative worldwide sales of the product, the Company will be required to pay to SLU a low single-digit royalty on net sales of the licensed products in any country or region, if such product sales are ever achieved.

#### **AAIPharma License Agreement**

In March 2011, the Company entered into a license agreement with AAIPharma Services Corp. (AAIPharma). Under the terms of this license agreement, AAI Pharma granted the Company a fully paid-up, royalty-free, exclusive, perpetual, and irrevocable license to research, develop, make, have made, use, import, offer for sale, and sell products incorporating AAIPharma's controlled release matrix solid dose oral tablet. Under the license agreement, the Company will pay a mid-single digit percentage of any sublicense revenue received by Ultragenyx related to the sublicense of AAIPharma technology that had been initially licensed by Ultragenyx.

#### **HIBM Research Group**

In April 2012, the Company entered into an exclusive license agreement with HIBM Research Group (HRG). Under the terms of this license agreement, HRG granted the Company an exclusive worldwide license to certain intellectual property related to the treatment of HIBM. The Company may make future payments that aggregate up to \$0.3 million that are contingent upon attainment of various development and approval milestones. Additionally, the Company will pay to HRG a royalty of less than 1% of net sales of the licensed products in the licensed territories, if such product sales are ever achieved.

#### **St. Jude Children's Research Hospital License Agreement**

In September 2012, the Company entered into a license agreement with St. Jude Children's Research Hospital (St. Jude). Under the terms of this license agreement, St. Jude granted the Company an exclusive license under certain know-how to research, develop, make, use, offer to sell, import, and otherwise commercialize and exploit St. Jude's protective protein, cathepsin, a protein product to treat, prevent, and/or diagnose galactosialidosis and other monogenetic diseases.

The Company will pay to St. Jude a royalty of less than 1% on net sales of the licensed products in the licensed territories, if such product sales are ever achieved.

#### **Baylor Research Institute License Agreement**

In September 2012, the Company entered into a license agreement with Baylor Research Institute (BRI). Under the terms of this license agreement, BRI exclusively licensed to the Company certain intellectual property related to triheptanoin for North America. In June 2013, the Company notified BRI that it was exercising its option pursuant to the agreement to license the rights to triheptanoin in all territories outside of the United States, Canada and Mexico and paid the option exercise fee of \$0.8 million.

The Company may make future payments of up to \$10.5 million contingent upon attainment of various development milestones and \$7.5 million contingent upon attainment of various sales milestones. Additionally, the Company will pay to BRI a mid-single digit royalty on net sales of the licensed product in the licensed territories, if such product sales are ever achieved.

**Kyowa Hakko Kirin Collaboration and License Agreement**

In August 2013, the Company entered into a collaboration and license agreement with Kyowa Hakko Kirin Co., Ltd. (KHK), which was amended in August 2015. Under the terms of this collaboration and license agreement, the Company and KHK will collaborate on the development and commercialization of certain products containing KRN23, an antibody directed towards FGF23, in the field of orphan diseases in the United States and Canada, or the profit share territory, and in the European Union, Switzerland, and Turkey, or the European territory, and the Company will have the right to develop and commercialize such products in the field of orphan diseases in Mexico and Central and South America, or Latin America. In the field of orphan diseases, and except for ongoing studies being conducted by KHK, the Company will be the lead party for development activities in the profit share territory and in the European territory until the applicable transition date; the Company will also be the lead party for core development activities conducted in Japan and Korea, provided that the core development plan related to Japan and Korea shall be limited to clinical trials mutually agreed to by the Company and KHK. The Company will share the costs for development activities in the profit share territory and European territory conducted pursuant to the development plan before the applicable transition date equally with KHK and KHK shall be responsible for 100% of the costs for development activities in Japan and Korea. On the applicable transition date in the profit share territory and the European territory, KHK will become the lead party and be responsible for the costs of the development activities. However, the Company will continue to share the costs of the studies commenced prior to the applicable transition date equally with KHK. The Company has the primary responsibility for conducting certain research and development services. The Company is obligated to provide assistance in accordance with the agreed upon development plan as well as participate on various committees. If KRN23 is approved, the Company and KHK will share commercial responsibilities and profits in the profit share territory until the applicable transition date, KHK will commercialize KRN23 in the European territory, and the Company will develop and commercialize KRN23 in Latin America. KHK will manufacture and supply KRN23 for clinical use globally and will manufacture and supply KRN23 for commercial use in the profit share territory and Latin America.

The Company is accounting for the agreement as a collaboration arrangement as defined in ASC 808, *Collaborative Agreements*; accordingly, the Company's expenses were reduced by \$10.8 million and \$4.0 million for reimbursable costs for the years ended December 31, 2015 and 2014, respectively, for its share of the costs as research and development. As of December 31, 2015 and 2014, the Company had receivables in the amount of \$3.8 million and \$1.3 million, respectively, for this collaboration arrangement.

**Arcturus Research Collaboration and License Agreement**

In October 2015, the Company entered into a Research Collaboration and License Agreement with Arcturus Therapeutics, Inc. (Arcturus). The Company and Arcturus will collaborate on the research and development of therapies for select rare diseases. As consideration for entering into the arrangement, the Company paid Arcturus an upfront fee of \$10.0 million. Arcturus will have the primary responsibility for conducting certain research services, funded by the Company, and the Company will be responsible for development and commercialization costs.

**6. Common Stock Warrants**

In connection with various financing activities, the Company issued preferred stock warrants. The Company determined the fair value of the warrants using an option-pricing method to allocate the equity value of the Company to the warrants based on the Company's capital structure. The equity value was estimated using the back-solve method, whereby the equity value was derived from a recent transaction involving the Company's own securities. The fair value ascribed to these warrants upon their issuance was \$0.2 million. Upon the closing of the Company's IPO in February 2014, the warrants were converted into warrants to purchase common stock. Accordingly, the warrants were reclassified from a liability to permanent equity and were no longer subject to remeasurement.

The table sets forth the outstanding common stock warrants for the years presented:

<b>Outstanding at December 31, 2015</b>	<b>Outstanding at December 31, 2014</b>	<b>Date Issued</b>	<b>Term</b>	<b>Exercise Price</b>
83,167	83,167	June 2010	10 years	\$ 3.006
—	174,651	February 2011	10 years	3.006
66,533	66,533	June 2011	10 years	3.006
<u>149,700</u>	<u>324,351</u>			

The fair value of the warrants was estimated to be \$6.7 million and \$3.4 million as of January 30, 2014 (pricing date of IPO) and December 31, 2013, respectively. The Company recorded \$0, \$3.3 million and \$2.9 million to other expense, net, for the years ended December 31, 2015, 2014 and 2013 respectively, representing the change in fair value of the warrants for the respective period.

**7. Common Stock**

The Company has reserved sufficient shares of common stock for issuance upon the exercise of stock options and the exercise of warrants. Common stockholders are entitled to dividends if and when declared by the board of directors, subject to the prior rights of the preferred stockholders. As of December 31, 2015, no common stock dividends had been declared by the board of directors.

The Company had reserved shares of common stock, on an as-converted basis, for future issuance as follows:

	<b>December 31,</b>	
	<b>2015</b>	<b>2014</b>
Common stock warrants outstanding	149,700	324,351
2011 equity incentive plan outstanding	1,212,931	1,960,225
2014 equity incentive plan outstanding	2,811,183	810,250
Shares available for future stock option grants	709,966	1,439,750
Employee stock purchase plan	950,295	600,000
	5,834,075	5,134,576

**8. Stock-Based Awards**

**2011 Equity Incentive Plan**

In 2011, the Company adopted the 2011 Equity Incentive Plan (the 2011 Plan). The 2011 Plan provides for the granting of stock-based awards to employees, directors, and consultants under terms and provisions established by the board of directors. Under the terms of the 2011 Plan, options may be granted at an exercise price not less than fair market value. For employees holding more than 10% of the voting rights of all classes of stock, the exercise prices for incentive stock options must be at least 110% of fair market of the common stock on the grant date, as determined by the board of directors. The terms of options granted under the 2011 Plan may not exceed ten years. Options granted generally vest over a period of four years. Typically, the vesting schedule for option grants to newly hired employees provides that 1/4 of the grant vests upon the first anniversary of the employee's date of hire, with the remainder of the shares vesting monthly thereafter at a rate of 1/48 of the total shares subject to the option. All other employee options typically vest in equal monthly installments over the four-year vesting schedule. In connection with the Company's IPO, no further grants subsequent to the IPO were made under this plan and all remaining shares available for grant were transferred to the 2014 Incentive Plan.

**2014 Incentive Plan**

In 2014, the Company adopted the 2014 Incentive Plan (the 2014 Plan), which became effective upon the closing of the Company's IPO in February 2014. The 2014 Plan had 2,250,000 shares of common stock available for future issuance at the time of its inception, which included 655,038 shares available under the 2011 Plan, which were transferred to the 2014 Plan upon adoption. The 2014 Plan provides for automatic annual increases in shares available for grant, beginning on January 1, 2015 through January 1, 2024. The 2014 Plan provides for the granting of stock-based awards to employees, directors, and consultants under similar terms, conditions and provisions as the 2011 Plan.

**Stock Option Activity**

The following table summarizes activity under the Company's stock option plans, including the 2011 Plan and the 2014 Plan and related information:

	<b>Options Outstanding</b>			
	<b>Number of Options</b>	<b>Weighted- Average Exercise Price</b>	<b>Weighted- Average Remaining Contractual Term (Years)</b>	<b>Aggregate Intrinsic Value</b>
				<b>(In thousands)</b>
Outstanding — December 31, 2012	1,520,967	\$ 0.47	9.11	\$ 2,038
Options granted	1,267,797	5.80		
Options exercised	(307,366)	0.55		
Options cancelled	(252,515)	1.26		
Outstanding — December 31, 2013	2,228,883	\$ 3.41	8.91	\$ 19,468
Options granted	932,555	41.12		
Options exercised	(305,090)	2.14		
Options cancelled	(116,873)	8.92		
Outstanding — December 31, 2014	2,739,475	\$ 16.15	8.43	\$ 79,840
Options granted	2,013,350	90.60		
Options exercised	(795,825)	8.65		
Options cancelled	(130,037)	31.49		
Outstanding — December 31, 2015	<u>3,826,963</u>	\$ 56.36	8.58	\$ 217,386
Vested and exercisable — December 31, 2015	<u>898,924</u>	\$ 13.30	7.14	\$ 88,886
Vested and expected to vest — December 31, 2015	<u>3,681,683</u>	\$ 55.27	8.56	\$ 212,968

The aggregate intrinsic values of options outstanding, vested and exercisable, and vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of the Company's common stock as of December 31, 2015. The total intrinsic value of options exercised during the years ended December 31, 2015, 2014 and 2013 was \$59.0 million, \$12.1 million and \$1.0 million, respectively. Cash received from the exercise of options was \$6.9 million, \$0.7 million, and \$0.2 million as of December 31, 2015, 2014, and 2013, respectively.

The options outstanding and exercisable by exercise price as of December 31, 2015 are as follows:

<b>Exercise Price</b>	<b>Options Outstanding</b>		<b>Options Exercisable</b>		
	<b>Numbers of Shares</b>	<b>Weighted- Average Remaining Contractual Term (in Years)</b>	<b>Numbers of Shares</b>	<b>Weighted- Average Exercise Price</b>	<b>Weighted- Average Remaining Contractual Term (in Years)</b>
\$0.31 to \$1.32	454,420	6.11	411,883	\$ 0.44	6.06
\$1.33 to \$9.03	542,555	7.67	222,173	5.26	7.68
\$9.04 to \$37.65	381,173	8.18	102,800	22.56	8.14
\$37.66 to \$53.33	334,273	8.78	77,966	45.83	8.54
\$53.34 to \$59.45	362,792	8.74	80,213	55.85	8.50
\$59.46 to \$79.33	188,500	9.33	3,889	59.95	9.27
\$79.34 to \$85.96	533,500	9.39	—	—	—
\$85.97 to \$98.72	339,750	9.56	—	—	—
\$98.73 to \$115.30	316,500	9.76	—	—	—
\$115.31 to \$131.47	373,500	9.61	—	—	—
	<u>3,826,963</u>	8.58	<u>898,924</u>	\$ 13.30	7.14

The weighted-average estimated fair value of stock options granted was \$54.90, \$26.58 and \$3.82 per share of the Company's common stock during the years ended December 31, 2015, 2014, and 2013, respectively.

The total estimated fair value of options vested during the years ended December 31, 2015, 2014 and 2013 was \$10.7 million, \$2.0 million, and \$0.1 million, respectively.

### Restricted Stock Units

In 2015 and 2014, the Company granted 187,260 and 31,000 Restricted Stock Units (RSUs) under the 2014 Plan to employees with a weighted-average grant date fair value of \$89.67 and \$53.23, respectively. The fair value of the RSUs is determined on the grant date based on the fair value of the Company's common stock. The fair value of the RSUs is recognized as expense ratably over the vesting period of two to four years. The total fair value of 18,209 shares vested during 2015 was approximately \$1.0 million with an aggregate intrinsic value of the shares of \$2.1 million. As of December 31, 2015, the total unrecognized compensation expense related to unvested RSUs, net of estimated forfeitures, was \$14.5 million, which the Company expects to recognize over an estimated weighted-average period of 3.4 years. The total outstanding RSUs at December 31, 2015 were 197,151 shares at a weighted-average grant date fair value of \$87.24.

### Employee Stock Purchase Plan

In January 2014, the Company adopted the 2014 Employee Stock Purchase Plan (the ESPP) which became effective upon the closing of our IPO in February 2014. The Company reserved a total of 600,000 shares of common stock for issuance under the ESPP. Eligible employees may purchase common stock at 85% of the lesser of the fair market value of common stock on the first or last day of the purchase period. The ESPP provides for automatic annual increases in shares available for grant, beginning on January 1, 2015 through January 1, 2024. The Company has not determined the date on which the initial purchase period will commence under the ESPP.

### Stock-Based Compensation Expense

Total stock-based compensation recognized was as follows (in thousands):

	<b>Year Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Research and development	\$ 17,100	\$ 4,116	\$ 293
General and administrative	7,784	1,278	364
<b>Total stock-based compensation expense</b>	<b>\$ 24,884</b>	<b>\$ 5,394</b>	<b>\$ 657</b>

As of December 31, 2015, the total unrecognized compensation expense related to 2.9 million unvested options, net of estimated forfeitures, was \$102.8 million, which the Company expects to recognize over an estimated weighted-average period of 3.25 years.

In determining the estimated fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

*Expected Term*—The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term).

*Expected Volatility*—Prior to the IPO in January 2014, the Company was privately held and did not have any trading history for its common stock; accordingly, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. In 2014, the Company modified its approach by phasing in our own common stock trading history and supplemented the remaining historical information with a blended volatility from the trading history from the common stock of the same set of comparable publicly traded biopharmaceutical companies. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available. Sufficient trading history does not yet exist for the Company's common stock, therefore the estimate of expected volatility is based on the volatility of other companies with similar products under development, market, size and other factors.

*Risk-Free Interest Rate*—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

*Expected Dividend*—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

**ULTRAGENYX PHARMACEUTICAL INC.**  
**Notes to Consolidated Financial Statements (continued)**

The fair value of stock option awards was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted-average assumptions:

	<b>Year Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Expected term	6.23 years	6.23 years	6.25 years
Expected volatility	65%	70%	74%
Risk-free interest rate	1.8%	1.9%	0.7% to 1.6%
Expected dividend rate	0.0%	0.0%	0.0%

**9. Defined Contribution Plan**

In March 2013, the Company began to sponsor a 401(k) retirement plan, in which substantially all of its full-time employees are eligible to participate. Eligible participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. Prior to 2015, the Company had not provided any contributions to the plan. In 2015, the Company began to make contributions to the Plan for eligible participants, and recorded \$0.6 million as contribution expenses for the year ended December 31, 2015.

**10. Income Taxes**

The Company did not record a provision or benefit for income taxes during the years ended December 31, 2015, 2014 and 2013. The Company has incurred net operating losses since inception. The Company has not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

The effective tax rate of our provision for income taxes differs from the federal statutory rate as follows:

	<b>Year Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Federal statutory income tax rate	34.0%	34.0%	34.0%
State income taxes, net of federal benefit	7.5	4.6	5.0
Federal tax credits	5.9	6.7	8.2
Other	0.8	—	—
Nondeductible permanent items	—	(1.2)	(2.9)
Stock compensation	(1.3)	(1.4)	(0.6)
Uncertain tax positions	(7.7)	—	0.9
Change in valuation allowance	(39.2)	(42.7)	(44.6)
Provision for income taxes	—	—	—

The tax effect of temporary differences that give rise to significant portions of the deferred tax assets is presented below (in thousands):

	<b>Year Ended December 31,</b>	
	<b>2015</b>	<b>2014</b>
<b>Deferred tax assets:</b>		
Net operating loss carryforwards	\$ 61,503	\$ 32,500
Tax credits	33,881	16,737
Stock options	6,680	1,058
Accruals and reserves	2,541	476
Fixed assets and intangibles	4,442	455
Other	432	113
Total deferred tax assets	109,479	51,339
Valuation allowance	(109,479)	(51,339)
Net deferred tax assets	\$ —	\$ —

As of December 31, 2015 and 2014, the Company had approximately \$225.5 million and \$89.0 million of federal net operating loss carryforwards available to reduce future taxable income that will begin to expire in 2030. As of December 31, 2015 and 2014, the Company had approximately \$255.0 million and \$90.1 million of state net operating loss carryforwards available to reduce future taxable income that will begin to expire in 2030.

**ULTRAGENYX PHARMACEUTICAL INC.**  
**Notes to Consolidated Financial Statements (continued)**

As of December 31, 2015 and 2014, the Company had federal research tax credit carryforwards of approximately \$1.7 million and \$1.0 million available to reduce future tax liabilities that will begin to expire in 2030. As of December 31, 2015 and 2014, the Company had state research credit carryforwards of approximately \$4.3 million and \$1.6 million available to reduce future tax liabilities that will be carried forward indefinitely.

As of December 31, 2015 and 2014, the Company had federal Orphan Drug Credits of approximately \$35.2 million and \$21.9 million available to reduce future tax liabilities that will begin to expire in 2030.

The Company's ability to use net operating loss and tax credit carryforwards to reduce future taxable income and liabilities may be subject to annual limitations pursuant to Internal Revenue Code Sections 382 and 383 as a result of ownership changes in the past and future. As a result of ownership changes in 2012 and 2011, \$3.3 million of federal net operating loss carryforwards, \$3.6 million of state net operating loss carryforwards, and \$0.3 million of federal tax credits are permanently limited. Deferred tax assets for net operating losses and tax credits have been reduced and a corresponding adjustment to the valuation allowance has been recorded.

The valuation allowance increased by \$58.1 million and \$25.6 million during the year ended December 31, 2015 and 2014, respectively.

The Company recorded unrecognized tax benefits for uncertainties in income taxes. A reconciliation of the Company's unrecognized tax benefits for the years ended December 31, 2015, 2014 and 2013 is as follows (in thousands):

	December 31,		
	2015	2014	2013
Balance at beginning of year	\$ 7,275	\$ 3,725	\$ 1,551
Additions based on tax positions related to current year	15,628	3,550	2,169
Additions for tax positions of prior years	5,505	—	—
Reductions for tax positions of prior years	(4,398)	—	5
Balance at end of year	<u>\$ 24,010</u>	<u>\$ 7,275</u>	<u>\$ 3,725</u>

The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized. The Company has elected to include interest and penalties as a component of tax expense. During the years ended December 31, 2015 and 2014, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits. The Company does not anticipate that the amount of existing unrecognized tax benefits will significantly increase or decrease during the next 12 months.

The Company files income tax returns in the U.S. federal, California, and other state tax jurisdictions. The federal and state income tax returns from inception to December 31, 2015 remain subject to examination.

## **11. Commitments and Contingencies**

### **Facilities**

In December 2015, the Company entered into a lease agreement for office facilities in Brisbane, California, which provided for a tenant improvement allowance of up to \$3.7 million. This operating lease is expected to commence in May 2016 and expires 122 months after the commencement date. At the end of the lease term, the Company has the option to extend the lease for two additional consecutive terms of five years each. As provided in the lease agreement, monthly lease payments are subject to annual increases as defined in the lease agreement.

Under the terms of the lease agreement and the addendum of its Brisbane office facility, the Company provided the lessor with an irrevocable letter of credit. The lessor shall be entitled to draw on the letter of credit in the event of any uncured default by the Company under the terms of the lease. Provided there has been no default on the lease, the Company may reduce the amount of the letter of credit by \$0.7 million on the fifth anniversary of the commencement date. As of December 31, 2015, the current amount of restricted cash and amount of the irrevocable letter of credit in connection with the lease agreement was \$1.4 million.

The Company leases office space and research, testing and manufacturing laboratory space in various facilities in Novato, California, under operating agreements expiring at various dates through 2020 and include tenant improvement allowance up to \$1.5 million. Certain of the leases provide for options by the Company to extend the lease for multiple five-year renewal periods and also provide for annual minimum increases in rent, usually based on a consumer price index or annual minimum increases.

Under the terms of the lease agreement and the addendum of its Novato office facility, the Company provided the lessor with an irrevocable letter of credit. The lessor shall be entitled to draw on the letter of credit in the event of any uncured default by the Company under the terms of the lease. Provided there has been no default on the lease, the Company may reduce the amount of the letter of credit by \$0.1 million on each anniversary date effective May 1, 2014. As of December 31, 2015, the current amount of restricted cash and amount of the irrevocable letter of credit in connection with the lease agreement was \$0.8 million.

The Company recognizes rent expense on a straight-line basis over the noncancelable term of its operating lease. Rent expense was \$1.4 million, \$0.6 million, and \$0.3 million during the years ended December 31, 2015, 2014 and 2013, respectively.

**ULTRAGENYX PHARMACEUTICAL INC.**  
**Notes to Consolidated Financial Statements (continued)**

**Other Commitments**

The Company has various manufacturing, clinical, research, and other contracts with vendors in the conduct of the normal course of its business. Other than as noted below, contracts are terminable, with varying provisions regarding termination. If a contract with a specific vendor were to be terminated, the Company would only be obligated for the products or services that the Company had received at the time the termination became effective.

As of December 31, 2015, the aggregate future minimum lease payments under the noncancelable operating lease arrangements and future payments under contractually binding manufacturing and service agreements are as follows (in thousands):

Year Ending December 31,	Leases	Manufacturing and Services
2016	\$ 2,270	\$ 2,042
2017	3,877	190
2018	4,504	90
2019	3,543	83
2020	2,868	62
Thereafter	13,791	—
	<u>\$ 30,853</u>	<u>\$ 2,467</u>

**Contingencies**

While there are no legal proceedings the Company is aware of, the Company may become party to various claims and complaints arising in the ordinary course of business. Management does not believe that any ultimate liability resulting from any of these claims will have a material adverse effect on its results of operations, financial position, or liquidity. However, management cannot give any assurance regarding the ultimate outcome of these claims, and their resolution could be material to operating results for any particular period, depending upon the level of income for the period.

**Guarantees and Indemnifications**

The Company indemnifies each of its directors and officers for certain events or occurrences, subject to certain limits, while the director is or was serving at the Company's request in such capacity, as permitted under Delaware law and in accordance with its certificate of incorporation and bylaws. The term of the indemnification period lasts as long as a director may be subject to any proceeding arising out of acts or omissions of such director in such capacity. The maximum amount of potential future indemnification is unlimited; however, the Company currently holds director liability insurance. This insurance allows the transfer of risk associated with the Company's exposure and may enable it to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, it has not recognized any liabilities relating to these obligations for any period presented.

**12. Net Loss per Share Attributable to Common Stockholders**

The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders during the years ended December 31, 2015, 2014 and 2013 (in thousands, except share and per share data):

	Year Ended December 31,		
	2015	2014	2013
<b>Numerator:</b>			
Net loss	\$ (145,618)	\$ (59,802)	\$ (35,070)
Accretion and dividends on convertible preferred stock	—	(4,808)	(15,219)
Net loss attributable to common stockholders	<u>\$ (145,618)</u>	<u>\$ (64,610)</u>	<u>\$ (50,289)</u>
<b>Denominator:</b>			
Weighted-average common shares outstanding	36,782,603	28,755,758	3,583,522
Less: weighted-average unvested common shares subject to repurchase	—	—	(201,033)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	<u>36,782,603</u>	<u>28,755,758</u>	<u>3,382,489</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (3.96)</u>	<u>\$ (2.25)</u>	<u>\$ (14.87)</u>

**ULTRAGENYX PHARMACEUTICAL INC.**  
**Notes to Consolidated Financial Statements (continued)**

The following weighted-average outstanding common stock equivalents were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented because including them would have been antidilutive:

	<b>Year Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Convertible preferred stock	—	1,610,834	19,598,486
Stock options to purchase common stock	3,247,925	2,572,729	1,666,036
Unvested restricted stock units	120,582	9,715	—
Common stock subject to repurchase	—	—	201,033
Convertible preferred stock warrants	—	29,051	353,459
Common stock warrants	195,762	318,666	—
	<u>3,564,269</u>	<u>4,540,995</u>	<u>21,819,014</u>

**13. Quarterly Financial Data (unaudited)**

The following table presents certain unaudited quarterly financial information. This information has been prepared on the same basis as the audited financial statements and includes all adjustments (consisting only of normal recurring adjustments) necessary to present fairly the unaudited quarterly results of operations set forth herein (in thousands, except share and per share data):

	<b>2015</b>			
	<b>March 31,</b>	<b>June 30,</b>	<b>September 30,</b>	<b>December 31,</b>
Operating expenses	\$ 21,502	\$ 30,142	\$ 39,936	\$ 56,158
Net loss	(21,379)	(29,787)	(39,232)	(55,220)
Net loss attributable to common stockholders	(21,379)	(29,787)	(39,232)	(55,220)
Net loss per share applicable to common stockholders, basic and diluted	\$ (0.63)	\$ (0.83)	\$ (1.03)	\$ (1.42)
	<b>2014</b>			
	<b>March 31,</b>	<b>June 30,</b>	<b>September 30,</b>	<b>December 31,</b>
Operating expenses	\$ 10,339	\$ 13,661	\$ 15,835	\$ 16,943
Net loss	(13,630)	(13,585)	(15,849)	(16,738)
Net loss attributable to common stockholders	(18,438)	(13,585)	(15,849)	(16,738)
Net loss per share applicable to common stockholders, basic and diluted	\$ (0.85)	\$ (0.45)	\$ (0.50)	\$ (0.52)

## Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed
		Form	Date	Number	Herewith
3.1	Amended and Restated Certificate of Incorporation	8-K	2/5/2014	3.1	
3.2	Amended and Restated Bylaws	8-K	2/5/2014	3.2	
4.1	Reference is made to Exhibits 3.1 and 3.2				
4.2	Form of Common Stock Certificate	S-1	11/8/2013	4.2	
4.3	Warrant, dated as of June 30, 2010, issued to Emil D. Kakkis, M.D., Ph.D.	S-1	11/8/2013	4.3	
4.4	Warrant, dated as of June 14, 2011, issued to Emil D. Kakkis, M.D., Ph.D.	S-1	11/8/2013	4.6	
4.5	Warrant, dated as of June 14, 2011, issued to Emil D. Kakkis, M.D., Ph.D.	S-1	11/8/2013	4.7	
4.6	Amended and Restated Investors' Rights Agreement, dated as of December 18, 2012, among the Registrant and the investors named therein	S-1	11/8/2013	4.8	
10.1†	Collaboration and License Agreement, dated as of August 29, 2013, between the Registrant and Kyowa Hakko Kirin Co., Ltd.	S-1	12/23/2013	10.1	
10.2	Amendment No. 1 to Collaboration and License Agreement, dated as of August 24, 2015, between the Registrant and Kyowa Hakko Kirin Co., Ltd.	10-Q	11/10/2015	10.2	
10.3†	License Agreement, dated as of March 1, 2011, between the Registrant and AAIPharma Services Corp.	S-1	12/23/2013	10.2	
10.4†	License Agreement, dated as of September 20, 2012, between the Registrant and Baylor Research Institute	S-1	12/23/2013	10.3	
10.5†	Amendment to the License Agreement, dated as of March 22, 2013, between the Registrant and Baylor Research Institute	S-1	11/8/2013	10.4	
10.6†	Exclusive License Agreement, dated as of April 23, 2012, between the Registrant and HIBM Research Group	S-1	11/8/2013	10.5	
10.7†	Collaboration and License Agreement, dated as of September 30, 2010, between the Registrant and Nobelpharma Co., Ltd.	S-1	12/23/2013	10.6	
10.8†	First Amendment to the Collaboration and License Agreement, dated August 10, 2015, between the Registrant and Nobelpharma Co., Ltd.	10-Q	11/10/2015	10.1	
10.9†	License Agreement, dated as of September 1, 2012, between the Registrant and St. Jude Children's Research Hospital	S-1	12/23/2013	10.7	
10.10	First Amendment to License Agreement, dated as of March 1, 2014, between the Registrant and St. Jude Children's Research Hospital	10-Q	8/11/2014	10.1	
10.11†	Exclusive License Agreement, dated as of November 22, 2010, between the Registrant and Saint Louis University	S-1	12/23/2013	10.8	
10.12†	Supply Agreement, dated as of November 19, 2012, between the Registrant and CREMER OLEO GmbH & Co KG	S-1	12/23/2013	10.9	
10.13†	Development and Clinical Supply Agreement, dated as of August 31, 2012, between the Registrant and Rentschler Biotechnologie GmbH	S-1	11/8/2013	10.10	
10.14	Amendment 1 to the Development and Clinical Supply Agreement, effective as of November 4, 2014, by and between the Registrant and Rentschler Biotechnologie GmbH	10-K	3/27/2015	10.34	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed
		Form	Date	Number	Herewith
10.15#	2011 Equity Incentive Plan (including forms of Stock Option Grant Notice and Stock Option Agreement thereunder)	S-1	11/8/2013	10.11	
10.16#	Amendment to the 2011 Equity Incentive Plan	S-1	11/8/2013	10.12	
10.17#	2014 Incentive Plan	S-1	1/17/2014	10.13	
10.18#	Form of Incentive Stock Option Agreement	S-1	1/17/2014	10.14	
10.19#	Form of Non Statutory Stock Option Agreement (Employees)	S-1	1/17/2014	10.15	
10.20#	Form of Non-Statutory Stock Option Agreement (Directors)	S-1	1/17/2014	10.16	
10.21#	Form of Restricted Stock Unit Agreement (Employees)	S-1	1/17/2014	10.17	
10.22#	Form of Restricted Stock Unit Agreement (Directors)	S-1	1/17/2014	10.18	
10.23#	2014 Employee Stock Purchase Plan	S-1	1/17/2014	10.19	
10.24#	Executive Employment Agreement, dated as of June 15, 2011, between the Registrant and Emil D. Kakkis, M.D., Ph.D.	S-1	11/8/2013	10.18	
10.25#	Amendment No. 1 to Executive Employment Agreement, dated August 8, 2014, by and between the Registrant and Emil D. Kakkis, M.D., Ph.D.	10-Q	8/11/2014	10.2	
10.26#	Offer Letter, dated as of October 31, 2011, between the Registrant and Thomas Kassberg	S-1	11/8/2013	10.19	
10.27#	Amendment No. 1 to Offer of Employment, dated as of August 8, 2014, by and between Ultragenyx Pharmaceutical Inc. and Thomas Kassberg	10-Q	8/11/2014	10.3	
10.28#	Offer Letter, dated as of March 12, 2012, between the Registrant and Shalini Sharp	S-1	11/8/2013	10.20	
10.29#	Amendment No. 1 to Offer of Employment, dated as of August 8, 2014, by and between Ultragenyx Pharmaceutical Inc. and Shalini Sharp	10-Q	8/11/2014	10.4	
10.30#	Offer Letter, dated as of June 17, 2014, between the Registrant and Sunil Agarwal, M.D.	10-Q	8/14/2015	10.1	
10.31#	Amendment No. 1 to Offer of Employment, dated as of August 8, 2014, by and between the Registrant and Sunil Agarwal, M.D.	10-Q	8/14/2015	10.2	
10.32#	Form of Indemnification Agreement	10-K	3/24/2014	10.23	
10.33	Standard Lease, dated as of July 5, 2011, between the Registrant and Condiotti Enterprises, Inc.	S-1	11/8/2013	10.22	
10.34	Addendum One to Standard Lease, dated as of July 5, 2011, between the Registrant and Condiotti Enterprises, Inc.				X
10.35	Addendum Two to Standard Lease, dated as of March 7, 2012, between the Registrant and Condiotti Enterprises, Inc.				X
10.36	Addendum #3 to Standard Lease, effective as of February 12, 2014, by and between the Registrant and Condiotti Enterprises, Inc.	8-K	2/25/2014	10.1	
10.37	Addendum #4 to Standard Lease, effective as of March 9, 2015, by and between the Registrant and Condiotti Enterprises, Inc.	8-K	3/13/2015	10.1	
10.38	Addendum #5 to Standard Lease, effective as of April 7, 2015, by and between the Registrant and Condiotti Enterprises, Inc.				X

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed
		Form	Date	Number	Herewith
10.39	License and Services Agreement, dated as of September 24, 2010, between the Registrant and The Buck Institute for Age Research	S-1	11/8/2013	10.23	
10.40	Amendment No. 1 to License and Services Agreement, dated as of September 4, 2012, between the Registrant and The Buck Institute for Research on Aging	S-1	11/8/2013	10.24	
10.41	Amendment No. 2 to License and Services Agreement, effective as of September 15, 2014, by and between the Registrant and The Buck Institute for Research on Aging	10-Q	11/10/2014	10.1	
10.42	Amendment No. 3 to License and Services Agreement, effective September 21, 2015, between the Registrant and The Buck Institute for Research on Aging	10-Q	11/10/2015	10.3	
10.43	Lease Agreement between Marina Boulevard Property, LLC and Ultragenyx Pharmaceutical Inc., dated as of December 8, 2015				X
10.44#	Corporate Bonus Plan	S-1	1/17/2014	10.27	
21.1	Subsidiaries of Ultragenyx Pharmaceutical Inc.				X
23.1	Consent of Independent Registered Public Accounting Firm				X
24.1	Power of Attorney (included on the signature page of this report)				
31.1	Certification of Chief Executive Officer of the Registrant, as required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X
31.2	Certification of Chief Financial Officer of the Registrant, as required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X
32.1*	Certification by the Chief Executive Officer and Chief Financial Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 36 of Title 18 of the United States Code (18 U.S.C. §1350)				X
101.INS	XBRL Instance Document				X
101.SCH	XBRL Taxonomy Extension Schema Document				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document				X

† Confidential treatment has been granted with respect to certain portions (indicated by asterisks) of this exhibit. Omitted portions have been filed separately with the SEC.

# Indicates management contract or compensatory plan.

\* The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

**Addendum One****44. Early Termination.**

In the event the Premises are not delivered within 150 to 180 days of the full execution of the Lease and said delay in delivery of the Premises is not the result of Lessee caused delays or force majeure, Lessee shall have a one time right to terminate this Lease subject to the following terms:

- a. Lessee shall provide Lessor with thirty (30) days written notification of its intent to terminate the Lease within 150 to 180 days of full execution of the Lease if the Premises are not delivered.
- b. All Lessee's deposits shall be returned to Lessee without offset or deduct, with the exception of monies deducted by Lessor from the Tenant Improvement fund to cover Lessor's Tenant Improvement expenditures to date.
- c. At such point, upon the return of any remaining deposits by Lessee, this Lease shall terminate and any and all obligations of the parties by or to each other shall expire.
- d. If such written notification is not received by Lessor by the above mentioned time period then this provision shall expire and Lessee shall have no further right to terminate the Lease.

**45. Letter of Credit.**

Throughout the initial term of the Lease, Lessee shall provide Lessor with an irrevocable Letter of Credit in the amount of \$376,000. The form and content of the Letter of Credit shall be approved by Lessor and attached as an exhibit to the Lease. The form of the Letter of Credit shall be such that it provides continuous security without allowing any risk of a gap in coverage. Such Letter of Credit to be issued Silicon Valley Bank who shall provide Lessor with local, same-day draw benefits upon presentation by Lessor of written demand therefore. This Letter of Credit is provided by Lessee as a material inducement for Lessor to enter into this Lease. Lessor and Lessee agree that in the event Lessee is in default under the Lease at any time or fails to complete the full initial term of the Lease that the amount of the Letter of Credit represents damage that Lessor will suffer, in addition to lost rents and damages recoverable under or arising from this Lease, due to being unable to fully recover the Tenant Improvement costs as herein provided. Lessor shall be entitled to draw on the Letter of Credit in the event of any uncured Default under this Lease, without separate or additional notice to Lessee. It shall be a default of the lease agreement if Lessee fails at any time during the initial term of this Lease, to maintain the Letter of Credit in the required amount.

Should Lessor draw against the Letter of Credit at any time during the Lease, Lessee shall within five (5) days, replace the Letter of Credit up to the amount required immediately prior to such draw.

It is agreed by Lessor and Lessee that no construction of Tenant Improvements shall commence unless and until Lessor has approved the language, form, and content of the Letter of Credit and Lessee has provided such Letter of Credit to Lessor.

Provided there has been no default by Lessee during the immediately preceding year and there has been or remains no Default under the Lease during the preceding twelve (12) months, Lessor shall upon each anniversary of the Commencement Date, reduce the amount of the Letter of Credit by an amount equal to \$75,200.00. At no time shall the amount of the Letter of Credit be reduced below \$75,200.00, which amount shall be continued as Deposit for the full and faithful performance of all Lease terms, conditions, and obligations throughout the entire term of the Lease, including any extensions to the initial term if so exercised.

**46. Environmental Phase 1 Listing Report.**

Prior to commencement of any construction on the Premises Lessor shall, at Lessor's sole cost and expense, order a Environmental Phase 1 Listing Report. Such report shall research previous uses of the Premises and related hazardous permits.

**47. Non-Disturbance, Attornment.**

Landlord shall use its best efforts to provide a non-disturbance agreement from the Building's lender, if there is a lender, in a form reasonably acceptable to the lender and Tenant. Landlord shall further agree that in event of any future financings during the term of the lease, that Landlord shall obtain a non-disturbance agreement from any and all future lenders in a form reasonably acceptable to the lender(s).

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#### **48. Access.**

From and after the Commencement Date as herein defined and throughout the term of the Lease Lessee will have access to the Building and the Premises seven (7) days per week, twenty-four (24) hours per day; subject to such rules and regulations as Lessor may reasonably require.

#### **49. Premises Measurement.**

Upon completion of the agreed Tenant Improvements, Lessor shall cause the Premises to be measured to BOMA Standards, including a 10% load factor for common areas.

#### **50. Expansion Space.**

Throughout the first 60 full months of this Lease, Tenant shall have a Right of First Offer to expand into any additional contiguous space within the Building. Tenant shall have Twenty-one (21) days to respond to Landlord's written notice to lease space that is within Tenant's First Offer rights. The Right of First Offer notice will be presented to Tenant by Landlord upon space becoming vacant and available to the market other than space that is vacant and deliverable by Landlord at the time the lease is executed. Any expansion space leased during the Tenant's first 60 full months of this Lease shall be at the then current rental rates and scheduled increases as the original lease, with a \$16.00 per square foot tenant improvement allowance for the office areas only, so long as Lessee retains the complete space (the initial space and all subsequent expansion space). Any expansion space leased after the 60<sup>th</sup> month of the initial term including any option periods shall be at 100% of fair market rent. Should Lessee exercise this Right of First Offer Space, the initial term of the Lease shall be extended to be not less than sixty (60) full months from commencement of additional space and shall include the entire initial space as well.

#### **51. Options to Extend.**

So long as Lessee is not in Default of the Lease, Lessee shall have two consecutive Options to Extend the Lease Term for a period of five years each, subject to the following terms:

- a. The Options to extend are personal to Lessee and are neither transferrable nor assignable to any other party;
- b. Lessee shall provide Lessor with not less than 6 months advance written notification of intent to exercise the Option. Should Lessor not receive such timely written notification, then the Option(s) shall expire.
- c. The Options to extend shall be consecutive to the initial term. If the first Option is not exercised, then both Options shall expire.
- d. The first year of the Option Term(s) shall be at the same Base Monthly Rent as the expiring 12 month period, where such Base Monthly Rent was for the identical space;
- e. Thereafter, the Base Monthly Rent shall be increased annually per the provisions of Section 8 of the Lease.
- f. Each party will bear the costs of any commissions incurred for such extension.
- g. The space shall be taken on an "As Is" basis, with no further allowance for Tenant Improvements.
- h. Lessee shall retain all of the space covered by the Lease and any expansions previously exercised.

#### **52. Tenant Improvements.**

(a) Costs. Lessor has agreed to provide a Tenant Improvement allowance of up to \$376,000 for the initial Premises ("Tenant Improvement Allowance"). The Tenant Improvement Allowance and Lessee's contribution for the overages in the Tenant Improvement costs shall be used by Lessor to pay the cost of the demolition, planning, design, engineering, permitting, construction and installation of the Tenant Improvements including, without limitation, fees and costs of the Architect (as defined below), Contractor (as defined below) and any other consultants (collectively, the "Tenant Improvement Costs") incurred in connection with the construction of all improvements shown in the Final Plans (as defined herein) (collectively, the "Tenant Improvements"). Such Tenant Improvements shall include, without limitation, interior walls for private offices, electrical outlets, lighting, acoustic tiles, paint, and roll-goods carpet, and necessary plans and permits, services of our general contractor and his staff, a construction management fee to be paid to Lessor in the amount of 4% of the total Tenant Improvement Costs (exclusive of said construction management fee).

Lessee has hired Steve Wisenbaker and Associates Architect to be its space plan designer whom shall complete the space plans which shall be provided to Lessor's engineer (the "final space plan") from which Lessor's engineer will prepare the construction documents for submittal to the City of Novato to acquire a building permit. Once the final space plan has been approved and

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signed off by both the Lessee and Lessor, and submitted to Lessor's engineer to commence construction drawing of the construction documents Lessee cannot make any changes to the plans without Lessor's prior, written consent. Lessor will fund the Tenant Improvement work as needed to complete the Tenant Improvements up Lessor's Tenant improvement allowance of \$376,000. To the extent the improvements exceed the Lessor's \$376,000 allowance Lessee, as a condition of this lease, shall be responsible to fund the completion of the improvements. Lessee shall pay to Lessor as billed by Lessor the progress payments for its share of the additional improvements within five (5) days of receipt of Lessor's bill to Lessee, and so on and so forth until the Tenant Improvements are complete and the Lessor has been paid in full by Lessee for that portion of the Tenant Improvements exceeding the Lessor's allowance of \$376,000. Notwithstanding any provision herein, Lessee cannot take occupancy of the Premises until Lessor has been paid in full. Lessee agrees that the Tenant Improvement allowance may not be used for personal items, including furniture, data lines, office equipment, phone lines, etc. Lessee shall not have access to the Premises before substantial completion of the Tenant Improvements without Lessor's advance, written approval.

(b) Lessee Architect. Lessee has selected and engaged Steve Wisenbaker and Associates as the architect for the Tenant Improvement Design (the "Architect").

(c) Space Plan. Lessor acknowledges that Lessee has provided Lessor and/or the Engineer with detailed final space plans ("Space Plan"), which Architect will use to prepare the Construction Drawings (as defined herein).

(d) Preparation and Approval of Construction Drawings. The Lessor's engineer shall complete working drawings (including all plans, specifications, construction documents and engineering) for the Lessee Improvements ("Construction Drawings") which shall be compatible with the Space Plan and with the design, construction and equipment of the Building, shall comply with all laws, statutes, ordinances, orders or governmental rule or regulations or requirements of duly constituted public authorities or quasi-public authorities in force at the time, shall be capable of logical measurement and construction, and shall contain all such information as may be required for the construction of the Tenant Improvements using building standard materials.

(f) Selection of Contractor. Lessor has selected MasterCraft Construction, Inc. to construct the Lessee Improvements based on the Space Plan (the "Contractor"). On or prior to the Lessor and Lessee making its first inspection of the Tenant Improvements Lessee shall designate in writing to Lessor one person to be the designated contact "Lessee Contact" to will do the walk through with the Lessor to inspect the Tenant Improvement work and creating a punch list as periodically requested by Lessor.

(g) Inspections. Upon Substantial Completion (as defined below) of the Tenant Improvements, Lessee and Lessor shall conduct a walk-through of the Premises and shall mutually agree upon a punch-list of items related to the Lessee Improvements, which punch-list items the Contractor will correct within thirty (30) days of such walk-through.

(h) Substantial Completion. "Substantial Completion" of the Tenant Improvements shall occur when the Lessee Improvements have been substantially completed in substantial compliance with the Final Plans, subject to "punch-list" items, the completion of which shall not unreasonably disturb Lessee's use of the Premises, and a Certificate of Occupancy has been issued by the City of Novato and Lessee has paid Lessor in the balance of the tenant improvement costs in excess of Lessor's Tenant Improvement allowance.

(i) Minor Change Orders. In the event that Lessee requests any changes to the Final Plans (a "Minor Change Order"), Lessor shall review and approve or disapprove such changes within three (3) business days after Lessor's receipt of Lessee's request, provided the changes do not create a Design Problem. For the purposes hereof, a "Design Problem" shall mean the following: (i) an adverse effect on the structural integrity of the Building; (ii) a reasonable likelihood of damage to the Building Systems; (iii) non-compliance with applicable codes; and (iv) failure to incorporate materials equal to or better than Building standard; (v) or **any change** which would require re-submittal to and/or result in additional fees due to the City of Novato or other agencies. Should Lessee request a Change Order, such request shall not delay the Lease Commencement Date. Further, to the extent the Tenant Improvement Allowance contains insufficient funds to perform such Change Order, Lessor and Contractor shall not commence work in connection with such Change Order unless and until such additional, certified funds are received from Lessee covering such additions, and Lessor.



**Addendum #5 To The Lease Dated on or about July 1, 2011****By and Between Condiotti Enterprises, Inc. ("Lessor") And****Ultragenyx Pharmaceutical Inc. ("Lessee")**

Lessor and Lessee are parties to that certain Lakepoint Business Park Standard Lease dated on or about July 1, 2011 and amended by that certain Addendum One dated on or about July 1, 2011, that certain Addendum Two dated on or about March 7, 2012, and that certain Addendum #3 effective February 12, 2014, pursuant to which Lessee leases from Lessor the entire space on the first and second floors of the building located at 60 Leveroni Court, Novato, California and Addendum #4 effective March 13, 2015 which adds the entire space at 52 Leveroni Court and which together constitute the Lease.

Now, therefore, the parties do wish to amend the Lease further as follows:

- 94.** Subject to the Terms of the Lease, there shall be added to the existing Premises occupied by Lessee (43,517sf±comprising the entire Building located at 60 Leveroni Court, and 20,343±sf comprising the entire Building located at 52 Leveroni Court, both in Novato, California) (the "Existing Space") approximately 10,408sf±, comprising the first floor of the Building located at 68 Leveroni Court. The Existing Space, the 52 Expansion Space and this additional space at 68 Leveroni Court (the "68 Expansion Space") are collectively referred to herein as the "Entire Premises".
- 95.** The Term for the 68 Expansion Space shall commence on May 1, 2015 and expire on April 30, 2019, unless extended in accordance with the Terms of the Lease.
- 96.** The Anniversary Date for the Entire Premises shall be May 1<sup>st</sup> for the purposes of the annual Base Monthly Rent increase, subject to the Terms of the Lease.
- 97.** Effective May 1, 2015 Initial Base Monthly Rent for the 52 Expansion Space shall be \$14,571.20.
- 98.** Thereafter, Base Monthly Rent for the Entire Premises shall be increased annually, effective May 1 of each year, in accordance with the Terms of the Lease.
- 99.** Lessee shall take the 68 Expansion Space in "As-Is" condition.
- 100.** Lessee shall not incur Base Monthly Rent for the period of early access, which shall commence upon full execution of this Addendum #5 and extend through April 30, 2015, but Lessee shall remain responsible for the prompt and timely payment of all utilities and other expenses incurred in connection with the early access to the 68 Expansion Space including Operating Expenses as detailed in Section 9 of the Lease.
- 101.** Lessor shall deliver the 68 Expansion Space with all Building Systems in good working condition.
- 102.** Lessee shall have exclusive use of up to 38 unreserved and unassigned parking spaces on the property.
- 103.** This 68 Expansion Space shall be eligible for the Options to Extend as included in Section 51 of the Lease and subject to those same Terms.
- 104.** Each party to this Addendum #5 represents and agrees that no commissions or fees of any kind have been incurred in relation to or as a result of this Addendum #5 and, further, any such commission or fee so related shall be borne by the party incurring it.
- 105.** Except as expressly modified by this Addendum #5 the Lease shall remain in full force and effect.

Agreed to this 7<sup>th</sup> day of April, 2015.

Lessee

Lessor

/s/ Emil Kakkis

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/s/ Jan Warz

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Emil Kakkis, President and CEO

Jan Warz, Vice President and COO

Ultragenyx Pharmaceutical Inc.

Condiotti Enterprises, Inc.

**LEASE AGREEMENT**  
**BETWEEN**  
**MARINA BOULEVARD PROPERTY, LLC,**  
**AS LANDLORD,**  
**AND**  
**ULTRAGENYX PHARMACEUTICAL INC.,**  
**AS TENANT**  
**DATED**  
**December 8, 2015**

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**List of Exhibits**

All exhibits and attachments attached hereto are incorporated herein by this reference. The following exhibits are attached to and made a part of this Lease:

- Exhibit A-1 - Site Plan Depicting Premises and Building
- Exhibit A-2 - Site Plan Depicting Complex
- Exhibit B - Legal Description of the Land
- Exhibit C - Additional Rent, Taxes and Insurance
- Exhibit D - Tenant Work Letter
- Exhibit E - Building Rules and Regulations
- Exhibit F - Form of Confirmation of Commencement Date Letter
- Exhibit G - Form of Tenant Estoppel Certificate
- Exhibit H - Renewal Option
- Exhibit I - Contractor Insurance Requirements
- Exhibit J - Environmental Questionnaire
- Exhibit K - Building Standards

**BASIC LEASE INFORMATION**

This Basic Lease Information is attached to and incorporated by reference to a Lease Agreement between Landlord and Tenant, as defined below.

Landlord: MARINA BOULEVARD PROPERTY, LLC,  
a Delaware limited liability company

Tenant: ULTRAGENYX PHARMACEUTICAL INC.,  
a Delaware corporation

Guarantor: None.

Premises: An area comprising the entire rentable square feet of the building commonly known as 5000 Marina Boulevard, Brisbane, California 94005 (the "**Building**"), which Building and Premises contains approximately 63,048 rentable square feet in the aggregate, as depicted on Exhibit A-1, comprised of (i) 19,684 rentable square feet on the 1st Floor, (ii) 21,662 rentable square feet on the 2nd Floor, and (iii) 21,702 rentable square feet on the 3rd Floor.

Land: The land on which the Building is located as described in Exhibit B.

Project: The Building, the Land and the driveways, parking facilities, and similar improvements and easements associated with the Building, Land and the operation thereof.

Complex: The Project and other buildings which comprise Marina Landing, a multi-building complex, subject to the conditions, covenants and restrictions as administered by owners' associations applicable to the Project, as further set forth and described in Exhibit A-2.

Term: One hundred twenty-two (122) months, commencing on the first day of the month following the Commencement Date (unless the Commencement Date is on the first day of the month, in which case the Term shall commence on the Commencement Date) and ending at 5:00 p.m. local time on the last day of the 122nd full calendar month following the Commencement Date, subject to adjustment and earlier termination as provided in the Lease.

Commencement Date: The earliest of: (a) the Substantial Completion of the initial Tenant Improvements in the Premises (including receipt of all required permits for the use thereof) as described in Exhibit D; or (b) the date the Tenant Improvements would have been substantially completed and the Premises would have been Ready For Occupancy except for Tenant Delays; or (c) occupancy of the Premises by Tenant for Tenant's business purposes; or (d) May 1, 2016. The terms "**Tenant Improvements**," "**Ready for Occupancy**" and "**Tenant Delays**" are defined in the Work Letter Agreement attached hereto as Exhibit D and made a part hereof.

Estimated Delivery Date: May 1, 2016

Base Rent:	Lease Month	Annual Base Rent	Monthly Base Rent	Monthly Rental Rate Per RSF
	1 – 12*	\$2,042,755.20	\$170,229.60	\$2.70
	13 – 24	\$2,103,281.20	\$175,273.44	\$2.78
	25 – 36	\$2,163,807.30	\$180,317.28	\$2.86
	37 – 48	\$2,231,899.20	\$185,991.60	\$2.95
	49 – 60	\$2,299,991.00	\$191,665.92	\$3.04
	61 – 72	\$2,368,082.80	\$197,340.24	\$3.13
	73 – 84	\$2,436,174.70	\$203,014.56	\$3.22
	85 – 96	\$2,511,832.30	\$209,319.36	\$3.32
	97 – 108	\$2,587,489.90	\$215,624.16	\$3.42
	109 – 120	\$2,663,147.50	\$221,928.96	\$3.52
	121 – 122	\$2,746,370.80	\$228,864.24	\$3.63

\* Monthly Base Rent shall be abated for the second (2nd) through and including the eleventh (11th) Lease Month pursuant to Section 4(b) of the Lease.

As used herein, the term “**Lease Month**” shall mean each calendar month during the Term (and if the Commencement Date does not occur on the first (1<sup>st</sup>) day of a calendar month, the period from the Commencement Date to the first (1<sup>st</sup>) day of the next calendar month shall be included in the first (1<sup>st</sup>) Lease Month for purposes of determining the duration of the Term and the monthly Base Rent rate applicable for such partial month).

Letter of Credit: \$1,373,185.40 (the amount of the Letter of Credit shall be subject to reduction as provided in Section 6).

Additional Rent: Tenant shall pay all costs of Common Area Maintenance Costs, Taxes and Insurance for the Building, and Tenant’s Proportionate Share of Common Area Maintenance Costs, Taxes, and Insurance for the Complex.

Utilities: Tenant shall obtain all water, electricity, sewerage, gas, telephone and other utilities for the Premises directly from the public utility company furnishing same. Any meters required in connection therewith shall be installed at Tenant’s sole cost.

Tenant’s Proportionate Share: For the Building - 100% of the Building.  
For the Complex – 41.80% of the Complex, which is the percentage obtained by dividing (a) the number of rentable square feet in the Building as stated above by (b) the rentable square feet in the buildings in the Complex at the time a respective charge was incurred, which at the time of execution of this Lease is 150,743 rentable square feet.

Permitted Use: For general office use, but for no other purpose whatsoever.

Tenant Improvements: Tenant accepts the Premises in its current “**AS-IS**” condition except that Landlord shall perform tenant improvements in the Premises in accordance with plans and specifications mutually approved by Landlord and Tenant under the terms and conditions as set forth in Exhibit D.

Parking: Tenant may use on a non-exclusive basis up to one hundred eighty-nine (189) undesignated automobile parking spaces in the parking area adjacent to the Building, at no cost to Tenant.

Minimum Insurance: Commercial General Liability Insurance with limits of not less than \$1,000,000 each occurrence and \$2,000,000 aggregate; Commercial Auto Liability Insurance with not less than \$1,000,000 combined single limit; Commercial Property Insurance on a replacement cost basis for Tenant’s personal property, fixtures, equipment and tenant improvements; Umbrella or Excess Liability Insurance with limits of not less than \$4,000,000 each occurrence and \$4,000,000 aggregate; Workers Compensation Insurance of not less than \$1,000,000; and Employer’s Liability Insurance with limits of not less than \$1,000,000 per accident.

Renewal Options: Tenant may renew this Lease for two (2) additional periods of five (5) years, by delivering written notice of the exercise thereof to Landlord not earlier than fifteen (15) months nor later than twelve (12) months before the expiration of the then-current Term, as further set forth in Exhibit H.

Broker/Agent: For Tenant: Savills-Studley, Inc.  
For Landlord: CBRE, Inc.

Tenant’s Address for Notices prior to Commencement Date: Ultragenyx Pharmaceutical Inc.  
60 Leveroni Court  
Novato, California 94949  
Attention: Chief Business Officer  
Telephone: (415) 483-8800  
Facsimile: (415) 483-8892  
  
With a copy to:  
Ultragenyx Pharmaceutical Inc.  
60 Leveroni Court  
Novato, California 94949  
Attention: Executive Director, Legal Affairs  
Telephone: (415) 483-8800  
Facsimile: (415) 483-8892

Tenant's Address for Notices after  
Commencement Date:

Ultragenyx Pharmaceutical Inc.  
5000 Marina Boulevard  
Brisbane, CA 94005  
Attention: Chief Business Officer  
Telephone: (415) 483-8800  
Facsimile: (415) 483-8892

with a copy to:

Ultragenyx Pharmaceutical Inc.  
60 Leveroni Court  
Novato, California 94949  
Attention: Executive Director, Legal Affairs  
Telephone: (415) 483-8800  
Facsimile: (415) 483-8892

Landlord's Address for Notices:

Marina Boulevard Property, LLC  
c/o Westport Capital Partners LLC  
2121 Rosecrans Avenue  
Suite 4325  
El Segundo, California 90245  
Attention: Eric Clapp, Managing Director  
Telephone: (310) 294-1239  
Facsimile: (310) 643-7379

With a copy to:

Marina Boulevard Property, LLC  
c/o Westport Capital Partners  
40 Danbury Road  
Wilton, Connecticut 06897  
Attention: Marc Porosoff, Esq.  
Telephone: (203) 429-8602  
Facsimile: (203) 429-8599

Additional copy to:

DLA Piper US LLP  
550 South Hope Street, Suite 2300  
Los Angeles, California 90071  
Attention: Jackie Park, Esq.  
Telephone: (213) 330-7743  
Facsimile: (213) 330-7543

Rent Payment Address:

Marina Boulevard Property, LLC  
c/o Sentinel Development  
18301 Von Karman, Suite 510  
Irvine, CA 92612

The foregoing Basic Lease Information is incorporated into and made a part of the Lease identified above. If any conflict exists between any Basic Lease Information and the Lease, then the Lease shall control.

## LEASE AGREEMENT

This Lease Agreement (this “**Lease**”) is entered into as of December 8, 2015, between MARINA BOULEVARD PROPERTY, LLC, a Delaware limited liability company (“**Landlord**”), and ULTRAGENYX PHARMACEUTICAL INC., a Delaware corporation (“**Tenant**”).

1. **Definitions and Basic Provisions.** The definitions and basic provisions set forth in the Basic Lease Information (the “**Basic Lease Information**”) executed by Landlord and Tenant contemporaneously herewith are incorporated herein by reference for all purposes. If any conflict exists between any Basic Lease Information and the Lease, then the Lease shall control. Additionally, the following terms shall have the following meanings when used in this Lease: “**Affiliate**” means any person or entity which, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with the party in question (as used herein, the term “control” shall mean the possession, direct or indirect, of not less than a majority of the voting rights attributable to the shares of Tenant and a majority of the outstanding capital stock of Tenant, or the power to direct or cause the direction of the management and policies of a Tenant, whether through the ownership of voting shares, by contract or otherwise); “**Building’s Structure**” means the Building’s exterior walls, roof, elevator shafts (if any), footings, foundations, structural portions of load-bearing walls, structural floors and subfloors, and structural columns and beams; “**Building’s Systems**” means the Premises’ and Building’s HVAC, life-safety, plumbing, electrical, and mechanical systems; “**Business Day(s)**” means Monday through Friday of each week, exclusive of Holidays; “**Complex**” shall collectively refer to the Building and any other buildings which comprise a multi-building complex owned by Landlord, if applicable and as further set forth in Exhibit A-1; “**Holidays**” means New Year’s Day, Memorial Day, Independence Day, Labor Day, Thanksgiving Day, Christmas Day, and any other nationally or regionally recognized holiday; “**including**” means including, without limitation; “**Land**” is the land on which the Building is located, as described on Exhibit B attached hereto; “**Laws**” means all federal, state, and local laws, ordinances, rules and regulations, all court orders, governmental directives, and governmental orders and all interpretations of the foregoing, and all restrictive covenants affecting the Project, and “**Law**” shall mean any of the foregoing; “**Project**” shall collectively refer to the Building, the Land and the driveways, parking facilities, and similar improvements and easements associated with the foregoing or the operation thereof; “**Rent**” shall collectively refer to Base Rent, Additional Rent, Taxes, and Insurance (each as defined in Exhibit C hereto), and all other sums that Tenant may owe to Landlord or otherwise be required to pay under the Lease; “**Tenant’s Off-Premises Equipment**” means any of Tenant’s equipment or other property that may be located on or about the Project (other than inside the Premises); and “**Tenant Party**” means any of the following persons: Tenant; any assignees claiming by, through, or under Tenant; any subtenants claiming by, through, or under Tenant; and any of their respective agents, contractors and employees.

2. **Lease Grant.** Subject to the terms of this Lease, Landlord leases to Tenant, and Tenant leases from Landlord, the Premises (as defined in the Basic Lease Information). The Premises are outlined on the plan attached to the Lease as Exhibit A.

### 3. **Tender of Possession; Square Footage of Premises.**

(a) **Tender of Possession.** Landlord and Tenant presently anticipate that possession of the Premises will be tendered to Tenant in the condition required by this Lease on or about the Estimated Delivery Date. If Landlord is unable to tender possession of the Premises in such condition to Tenant by the Estimated Delivery Date, then: (i) the validity of this Lease shall not be affected or impaired thereby; (ii) Landlord shall not be in default hereunder or be liable for damages therefor; and (iii) Tenant shall accept possession of the Premises when Landlord tenders possession thereof to Tenant. If for any reason Landlord has not delivered possession of the Premise in the condition required by this Lease on or before November 1, 2016 as extended below (the “**Outside Delivery Date**”), Tenant shall have the right to terminate this Lease by delivery to Landlord of a notice (the “**Termination Notice**”), which termination shall be effective ten (10) business days after Tenant’s delivery of the Termination Notice to Landlord, unless within such ten (10) business day period Landlord shall deliver to Tenant the Premises in the condition required by this Lease. In the event Tenant shall elect to terminate this Lease as set forth herein by delivery of the Termination Notice to Landlord and Landlord shall not have delivered to Tenant the Premises in the condition required by this Lease within such ten (10) business day period, then Landlord shall promptly return the Letter of Credit to Tenant and neither Landlord nor Tenant shall have any further obligation to the other under this Lease. The Outside Delivery Date shall be extended one (1) day for each day of Tenant Delay (as hereinafter defined in the Tenant Work Letter attached hereto as Exhibit D) and Force Majeure Event (as hereinafter defined in Section 26(c)). By occupying the Premises, Tenant shall be deemed to have accepted the Premises in their condition as of the date of such occupancy, subject to the performance of punch-list items that remain to be performed by Landlord, if any. The date that the Premises are actually tendered to Tenant shall be referred to herein as the “**Delivery Date**.” Within ten (10) Business Days following the Commencement Date, Tenant shall execute and deliver to Landlord a letter substantially in the form of Exhibit F hereto confirming: (1) the Commencement Date (as defined in the Basic Lease Information) and the expiration date of the initial Term (as defined in the Basic Lease Information); (2) that Tenant has accepted the Premises; and (3) that Landlord has performed all of its obligations with respect to the Premises (except for punch-list items specified in such letter); however, the failure of the parties to execute such letter shall not defer the Commencement Date or otherwise invalidate this Lease. Tenant’s failure to execute such document within ten (10) days of receipt thereof from Landlord shall be deemed Tenant’s agreement to the contents of such document. Any use of the Premises by Tenant prior to the Commencement Date shall be subject to all of the provisions of this Lease excepting only those requiring the payment of Rent.

(b) **Square Footage of Premises.** For purposes of this Lease, the “rentable square feet” of the Premises and the Complex has been calculated by Landlord pursuant to the Building Owners and Managers Association International Standard Method for Measuring Floor Area in Office Buildings, ANSI Z65.1 - 2010 (the “**BOMA Standard**”). The rentable square footage of the Premises set forth in this Lease shall be deemed by Tenant to be the rentable square footage of the Premises for all purposes. In that regard, Tenant has been given an opportunity to measure the rentable square footage of the Premises prior to execution of this Lease and Tenant hereby waives any rights it may have following execution of this Lease to measure the Premises or claim that the rentable square footage of the Premises is other than as set forth in this Lease.

#### 4. **Rent; Abatement of Rent.**

(a) **Rent.** Tenant shall timely pay to Landlord Rent, including the amounts set forth in Exhibit C hereto, without notice, demand, deduction or set-off (except as otherwise expressly provided herein), by good and sufficient check drawn on a national banking association at Landlord’s address provided for in this Lease or electronically via automatic debit or wire transfer to such account as Landlord designates in writing to Tenant, or as otherwise specified by Landlord. The obligations of Tenant to pay Base Rent (as defined in the Basic Lease Information) and other sums to Landlord and the obligations of Landlord under this Lease are independent obligations. Base Rent shall be payable monthly in advance. The first (1st) monthly installment of Base Rent shall be payable contemporaneously with the execution of this Lease; thereafter, Base Rent shall be payable on the first (1st) day of each month beginning on the first (1st) day of the second (2nd) full calendar month of the Term. The monthly Base Rent for any partial month at the beginning of the Term shall equal the product of 1/365 of the annual Base Rent in effect during the partial month and the number of days in the partial month, and shall be due on the Commencement Date. Payments of Base Rent for any fractional calendar month at the end of the Term shall be similarly prorated. Tenant shall pay Additional Rent, Taxes and Insurance (each as defined in Exhibit C) at the same time and in the same manner as Base Rent.

(b) **Abatement of Rent.** Notwithstanding anything to the contrary contained herein and provided that Tenant faithfully performs all of the terms and conditions of this Lease, Landlord hereby agrees to abate Tenant’s obligation to pay Tenant’s monthly Base Rent (the “**Abated Rent**”) for the second (2nd) through and including eleventh (11th) Lease Month of the initial Term (the “**Abatement Period**”), which total amount of Abated Rent is \$1,702,296.00 (i.e., 10 months x \$170,229.60 per month = \$1,702,296.00). During the Abatement Period, Tenant shall remain responsible for the payment of all of its other monetary obligations under this Lease. If at any time during the Term an Event of Default by Tenant occurs (as defined in Section 17 below), all Abated Rent that is unamortized as of the occurrence of the Event of Default (such amortization to be computed over the number of full calendar months in the Term of the Lease from and after the Abatement Period through the expiration of the Term of the Lease, together with interest thereon at a rate equal to eight percent (8%) per annum) shall become immediately due and payable by Tenant to Landlord. The payment by Tenant of the unamortized portion of the Abated Rent following the occurrence of an Event of Default shall not limit or affect any of Landlord’s other rights or remedies upon the occurrence of an Event of Default by Tenant, whether pursuant to the Lease or at law or in equity.

5. **Delinquent Payment; Handling Charges.** All past due payments required of Tenant hereunder shall bear interest from the date due until paid at the lesser of the “prime” rate as published in the Wall Street Journal plus two percent (2%) per annum or the maximum lawful rate of interest (such lesser amount is referred to herein as the “**Default Rate**”); additionally, Landlord, in addition to all other rights and remedies available to it, may charge Tenant a fee equal to five percent (5%) of the delinquent payment to reimburse Landlord for its cost and inconvenience incurred as a consequence of Tenant’s delinquency. In no event, however, shall the charges permitted under this Section 5 or elsewhere in this Lease, to the extent they are considered to be interest under applicable Law, exceed the maximum lawful rate of interest.

Notwithstanding the foregoing, the foregoing late charge shall be waived for the first such late payment of Rent or other charges during each twelve (12) month period for the Term of this Lease, provided, that, such payment is made within ten (10) days of the date such payment is due.

6. **Letter of Credit.** Tenant shall deliver to Landlord, no later than 5:00 p.m. PST December 11, 2015, a Letter of Credit (as hereinafter defined) in the amount specified in the Basic Lease Information, as additional security for the faithful performance and observance by Tenant of the terms, covenants and conditions of this Lease. The Letter of Credit shall be in the form of a clean, irrevocable, non-documentary and unconditional letter of credit (the “**Letter of Credit**”) issued by and drawable upon any commercial bank, trust company, national banking association or savings and loan association with offices for banking purposes in Los Angeles, California and otherwise satisfactory to Landlord (the “**Issuing Bank**”), which has outstanding unsecured, uninsured and unguaranteed indebtedness, or shall have issued a letter of credit or other credit facility that constitutes the primary security for any outstanding indebtedness (which is otherwise uninsured and unguaranteed), that is then rated, without regard to qualification of such rating by symbols such as “+” or “-” or numerical notation, “Aa” or better by Moody’s Investors Service and “AA” or better by Standard & Poor’s Rating Service, and has combined capital, surplus and undivided profits of not less than \$2,000,000,000. The Letter of Credit shall (a) name Landlord as beneficiary, (b) have a term of not less than one (1) year, (c) permit multiple drawings, (d)

be fully transferable by Landlord without the payment of any fees or charges by Landlord, and (e) otherwise be in form and content satisfactory to Landlord. The Letter of Credit shall provide that it shall be deemed automatically renewed, without amendment, for consecutive periods of one year each thereafter during the Term (and in no event shall the Letter of Credit expire prior to the forty-fifth (45th) day following the Expiration Date) unless the Issuing Bank sends duplicate notices (the “**Non-Renewal Notices**”) to Landlord by certified mail, return receipt requested (one of which shall be addressed “Attention, Chief Legal Officer” and the other of which shall be addressed “Attention, Chief Financial Officer”), not less than forty-five (45) days next preceding the then expiration date of the Letter of Credit stating that the Issuing Bank has elected not to renew the Letter of Credit. The Issuing Bank shall agree with all drawers, endorsers and bona fide holders that drafts drawn under and in compliance with the terms of the Letter of Credit will be duly honored upon presentation to the Issuing Bank at an office location in Los Angeles, California. The Letter of Credit shall be subject in all respects to the International Standby Practices 1998, International Chamber of Commerce Publication No. 590.

Effective on the fifth (5<sup>th</sup>) anniversary of the Commencement Date (“**Reduction Date**”) and as long as the Reduction Conditions (as hereinafter defined) have been satisfied by Tenant, the amount of the Letter of Credit shall be reduced to an amount equal to Six Hundred Eighty-Six Thousand Five Hundred Ninety-Two and 72/100 Dollars (\$686,592.72). For purposes of this Section 6, the “**Reduction Conditions**” shall mean (a) no Event of Default has occurred under this Lease from the Commencement Date through and including the Reduction Date, and (b) for the thirty (30) day period ending on the Reduction Date, Tenant has maintained market capitalization above \$2.0 Billion Dollars, as indicated on NASDAQ.

(a) Application of Security. If (a) an event of default by Tenant occurs in the payment or performance of any of the terms, covenants or conditions of this Lease, including the payment of Rent, or (b) Tenant fails to make any installment of Rent as and when due, or (c) Landlord receives a Non-Renewal Notice, Landlord shall have the right by sight draft to draw, at its election, all or a portion of the proceeds of the Letter of Credit and thereafter hold, use, apply, or retain the whole or any part of such proceeds, as the case may be, (x) to the extent required for the payment of any Rent or any other sum as to which Tenant is in default including (i) any sum which Landlord may expend or may be required to expend by reason of Tenant’s default, and/or (ii) any damages to which Landlord is entitled pursuant to this Lease, whether such damages accrue before or after summary proceedings or other reentry by Landlord, and/or (y) as a cash security deposit, unless and until, in the case of clause (c) above, Tenant delivers to Landlord a substitute Letter of Credit which meets the requirements of this Section 6. If Landlord applies or retains any part of the proceeds of the Letter of Credit, or cash security, Tenant, upon demand, shall deposit with Landlord the amount so applied or retained so that Landlord shall have the full amount thereof on hand at all times during the Term. If Tenant shall comply with all of the terms, covenants and conditions of this Lease, the Letter of Credit or cash security, as the case may be, shall be returned to Tenant not later than sixty (60) days after the Expiration Date and after delivery of possession of the Premises to Landlord in the manner required by this Lease.

(b) Transfer. Upon a sale or other transfer of the Building, or any financing of Landlord’s interest therein, Landlord shall have the right to transfer the Letter of Credit or the cash security to its transferee or lender. With respect to the Letter of Credit, within five (5) days after notice of such transfer or financing, Tenant, at its sole cost, shall arrange for the transfer of the Letter of Credit to the new landlord or the lender, as designated by Landlord in the foregoing notice or have the Letter of Credit reissued in the name of the new landlord or the lender. Upon such transfer, Tenant shall look solely to the new landlord or lender for the return of the Letter of Credit or such cash security and the provisions hereof shall apply to every transfer or assignment made of the Letter of Credit or such cash security to a new landlord. Tenant shall not assign or encumber or attempt to assign or encumber the Letter of Credit or such cash security and neither Landlord nor its successors or assigns shall be bound by any such action or attempted assignment, or encumbrance.

## 7. Services; Utilities; Common Areas.

(a) Services. Other than Landlord’s maintenance obligations expressly set forth in this Lease, Landlord shall not be obligated to provide any services to Tenant.

(b) Excess Utility Use. Tenant shall obtain all water, electricity, sewerage, gas, telephone and other utilities for the Premises directly from the public utility company furnishing same. Any meters required in connection therewith shall be installed at Tenant’s sole cost. Tenant shall pay all utility deposits and fees, and all monthly service charges for water, electricity, sewage, gas, telephone and any other utility services furnished to the Premises during the Term of this Lease. Tenant shall not install any equipment which exceeds or overloads the capacity of the utility facilities serving the Premises. If Tenant uses heat or air conditioning systems in excess of an average of sixty (60) hours per calendar week over a three (3) month period, Tenant shall pay to Landlord, upon billing, the cost of the increased wear and tear on existing equipment (including without limitation, the accelerated depreciation thereof) caused by such excess consumption as determined by Landlord. Amounts payable by Tenant to Landlord for such excess use of heat or air conditioning systems shall be deemed Additional Rent hereunder and shall be billed on a monthly basis.

(c) **Common Areas.** The term “**Common Area**” is defined for all purposes of this Lease as that part of the Project and/or Complex intended for the common use of all tenants, including among other facilities (as such may be applicable to the Complex), parking areas, private streets and alleys, landscaping, curbs, loading areas, sidewalks, lighting facilities, drinking fountains, meeting rooms, public toilets, and the like, but excluding: (i) space in buildings (now or hereafter existing) designated for rental for commercial purposes, as the same may exist from time to time; (ii) streets and alleys maintained by a public authority; (iii) areas within the Complex which may from time to time not be owned by Landlord (unless subject to a cross-access or common use agreement benefiting the area which includes the Premises); and (iv) areas leased to a single-purpose user where access is restricted. In addition, although the roof(s) of the building(s) in the Complex is not literally part of the Common Area, it will be deemed to be so included for purposes of: (x) Landlord’s ability to prescribe rules and regulations regarding same; and (y) its inclusion for purposes of Common Area Maintenance reimbursements. Landlord reserves the right to change from time to time the dimensions and location of the Common Area, as well as the dimensions, identities, locations and types of any buildings, signs or other improvements in the Complex, so long as access to the Premises is not materially adversely affected thereby. Tenant, and its employees and customers, and when duly authorized pursuant to the provisions of this Lease, its subtenants, licensees and concessionaires, shall have the non-exclusive right to use the parking spaces designated in the Basic Lease Information in the Common Area (excluding roof(s)) as constituted from time to time, such use to be in common with Landlord, other tenants in the Building and/or Complex, as applicable, and other persons permitted by the Landlord to use the same, and subject to rights of governmental authorities, easements, other restrictions of record, and such reasonable rules and regulations governing use as Landlord may from time to time prescribe. For example, and without limiting the generality of Landlord’s ability to establish rules and regulations governing all aspects of the Common Area, Tenant agrees as follows:

(i) Landlord may from time to time designate specific areas within the Project or Complex, as applicable, or in reasonable proximity thereto in which automobiles owned by Tenant, its employees, subtenants, licensees, and concessionaires shall be parked, provided that such designated parking spaces will at all times accommodate not fewer than 189 automobiles; and Tenant agrees that if any automobile or other vehicle owned by Tenant or any of its employees, its subtenants, its licensees or its concessionaires, or their employees, shall at any time be parked in any part of the Project or Complex, as applicable, other than the specified areas designated for employee parking, Landlord may have such vehicle towed at the cost of the owner of same.

(ii) Tenant shall not solicit business within the Common Area nor take any action which would interfere with the rights of other persons to use the Common Area.

(iii) Landlord may temporarily close any part of the Common Area for such periods of time as may be necessary to make repairs or alterations or to prevent the public from obtaining prescriptive rights, so long as access to the Premises is not materially adversely affected thereby and Tenant has the ability at all times to park not fewer than 189 automobiles.

(iv) With regard to the roof(s) of the building(s) in the Project or Complex, as applicable, use of the roof(s) is reserved to Landlord, or with regard to any tenant demonstrating to Landlord’s satisfaction a need to use same, to such tenant after receiving prior written consent from Landlord.

(v) Tenant shall have the right, at its sole cost and expense, to designate and mark twelve (12) parking spaces located in close proximity to the front door of the Building as reserved parking for Tenant’s visitors, which twelve (12) parking spaces are part of and included within the one hundred eighty-nine (189) parking spaces provided by Landlord to Tenant under this Lease. Tenant hereby acknowledges and agrees that (a) Tenant shall be responsible at its sole cost and expense for designating and marking such twelve (12) parking spaces and for monitoring the use thereof by Tenant’s visitors, and (b) Landlord shall have no responsibility or obligation for monitoring such parking spaces for Tenant’s visitors.

#### 8. **Alterations; Repairs; Maintenance; Signs.**

(a) **Alterations.** Tenant shall not make any alterations, additions or improvements to the Premises (collectively, the “**Alterations**”) without the prior written consent of Landlord, which consent shall not be unreasonably withheld, conditioned or delayed, except for the installation of unattached, movable trade fixtures which may be installed without drilling, cutting or otherwise defacing the Premises. Tenant shall furnish complete plans and specifications to Landlord for its approval, which approval shall not be unreasonably withheld, conditioned or delayed, at the time it requests Landlord’s consent to any Alterations if the desired Alterations: (i) will affect the Building’s Systems or Building’s Structure; or (ii) will require the filing of plans and specifications with any governmental or quasi-governmental agency or authority; or (iii) will require a building permit or other federal, state, county or local approvals with respect thereto; or (iv) will cost in excess of Ten Thousand Dollars (\$10,000.00). Subsequent to obtaining Landlord’s consent and prior to commencement of the Alterations, Tenant shall deliver to Landlord any building permit required by applicable Law and a copy of the executed construction contract(s). Tenant shall reimburse Landlord within ten (10) days after the rendition of a bill for all of Landlord’s reasonable out-of-pocket costs incurred in connection with any Alterations, including all management, engineering, outside consulting, and construction fees incurred by or on behalf of Landlord for the review and approval of Tenant’s plans and specifications and for the

monitoring of construction of the Alterations, together with a supervision coordination fee to Landlord in an amount equal to the product of (i) four percent (4%) and (ii) the costs of the Alterations. If Landlord consents to the making of any Alteration, such Alteration shall be made by Tenant at Tenant's sole cost and expense by contractors and subcontractors approved in writing by Landlord in accordance with Section 8(b)(iii), which approval shall not unreasonably be withheld, conditioned or delayed. All Alterations shall conform, at a minimum, to the Building Standards attached hereto as Exhibit K, as the same may be modified by Landlord from time to time (the "**Building Standards**"). Without Landlord's prior written consent, Tenant shall not use any portion of the Common Areas either within or without the Project or Complex, as applicable, in connection with the making of any Alterations. If the Alterations which Tenant causes to be constructed result in Landlord being required to make any alterations and/or improvements to other portions of the Project or Complex, as applicable, in order to comply with any applicable Laws, then Tenant shall reimburse Landlord upon demand for all costs and expenses incurred by Landlord in making such alterations and/or improvements. Any Alterations made by Tenant shall become the property of Landlord upon installation and shall remain on and be surrendered with the Premises upon the expiration or sooner termination of this Lease, except Tenant shall upon demand by Landlord, at Tenant's sole cost and expense, forthwith and with all due diligence (but in any event not later than ten (10) days after the expiration or earlier termination of the Lease) remove all or any portion of any Alterations made by Tenant which are designated by Landlord to be removed (including without limitation stairs, bank vaults, and cabling, if applicable) and repair and restore the Premises in a good and workmanlike manner to their original condition, reasonable wear and tear and casualty not required to be repaired by Tenant excepted. Notwithstanding the foregoing, upon Tenant's request at the time it seeks Landlord's consent to an Alteration, Landlord agrees to indicate in writing whether it will require such Alteration to be removed upon the expiration or earlier termination of the Lease. All construction work done by Tenant within the Premises shall be performed in a good and workmanlike manner with new materials of first-class quality, lien-free and in compliance with all Laws, and in such manner as to cause a minimum of interference with other construction in progress and with the transaction of business in the Project or Complex, as applicable. **TENANT AGREES TO INDEMNIFY, DEFEND AND HOLD LANDLORD HARMLESS AGAINST ANY LOSS, LIABILITY OR DAMAGE RESULTING FROM SUCH WORK, AND TENANT SHALL, IF REQUESTED BY LANDLORD, FURNISH A BOND OR OTHER SECURITY SATISFACTORY TO LANDLORD AGAINST ANY SUCH LOSS, LIABILITY OR DAMAGE (PROVIDED, HOWEVER, THAT NO BOND SHALL BE REQUIRED AS LONG AS NO EVENT OF DEFAULT SHALL HAVE OCCURRED UNDER THIS LEASE).** The foregoing indemnity shall survive the expiration or earlier termination of this Lease. Landlord's consent to or approval of any Alterations, additions or improvements (or the plans therefor) shall not constitute a representation or warranty by Landlord, nor Landlord's acceptance, that the same comply with sound architectural and/or engineering practices or with all applicable Laws, and Tenant shall be solely responsible for ensuring all such compliance.

Notwithstanding the foregoing, Tenant shall not be obligated to receive the written consent of Landlord for interior Alterations to the Premises (i) where the estimated cost of the proposed Alteration is Fifty Thousand Dollars (\$50,000.00) or less, (ii) if said Alterations do not affect the structural components of the Building, or adversely affect the systems and equipment or which can be seen from outside the Premises, or (iii) if said Alteration shall not require a building permit or any federal, state, county or local approvals.

**(b) Repairs; Maintenance.**

(i) **By Landlord.** Landlord shall, subject to reimbursement under Exhibit C, keep the foundation, the exterior walls (except plate glass; windows, doors and other exterior openings; window and door frames, molding, closure devices, locks and hardware; special store fronts; lighting, heating, air conditioning, plumbing and other electrical, mechanical and electromotive installation, equipment and fixtures; signs, placards, decorations or other advertising media of any type; and interior painting or other treatment of exterior walls), and roof structure of the Premises in good repair. Landlord, however, shall not be required to repair any damage resulting from the act or negligence of Tenant, its agents, contractors, employees, subtenants, licensees and concessionaires (including, but not limited to, roof leaks resulting from Tenant's installation of air conditioning equipment or any other roof penetration or placement); and the provisions of the previous sentence are expressly recognized to be subject to the casualty and condemnation provisions of this Lease. In the event that the Premises should become in need of repairs required to be made by Landlord hereunder, Tenant shall give prompt written notice thereof to Landlord and Landlord shall have a reasonable time after receipt by Landlord of such written notice in which to make such repairs. Landlord shall not be liable to Tenant for any interruption of Tenant's business or inconvenience caused due to any work performed in the Premises or in the Complex pursuant to Landlord's rights and obligations under the Lease, provided, however, Landlord shall use commercially reasonable efforts to not disturb the normal conduct of Tenant's business while performing such repairs and maintenance. In addition, Landlord shall maintain the Common Areas of the Project or Complex, as applicable, subject to reimbursement as set forth in Exhibit C. **TENANT HEREBY WAIVES AND RELEASES ITS RIGHT TO MAKE REPAIRS AT LANDLORD'S EXPENSE UNDER SECTIONS 1941 AND 1942 OF THE CALIFORNIA CIVIL CODE OR UNDER ANY SIMILAR LAW, STATUTE OR ORDINANCE NOW OR HEREAFTER IN EFFECT.**

(ii) **By Tenant.** Tenant shall keep the Premises in good, clean and habitable condition and shall at its sole cost and expense keep the same free of dirt, rubbish, ice or snow, insects, rodents, vermin and other pests and make all needed repairs and replacements, including replacement of cracked or broken glass, except for repairs and replacements required to be made by Landlord.

Without limiting the coverage of the previous sentence, but subject to the limitation set forth in the following sentence, it is understood that Tenant's responsibilities therein include the repair and replacement in accordance with all applicable Laws of all lighting, heating, air conditioning, plumbing and other electrical, mechanical and electromotive installation, equipment and fixtures and also include all utility repairs in ducts, conduits, pipes and wiring, and any sewer stoppage located in, under and above the Premises, regardless of when or how the defect or other cause for repair or replacement occurred or became apparent. All repairs by Tenant shall conform, at a minimum, to the Building Standards attached hereto as Exhibit K, as the same may be modified by Landlord from time to time. All contractors and subcontractors shall be subject to Landlord's written approval in accordance with Section 8(b)(iii). If any repairs required to be made by Tenant hereunder are not made or commenced within ten (10) days after written notice delivered to Tenant by Landlord (such time period not being subject to the notice and cure provisions of Section 17(f)), Landlord may at its option make such repairs without liability to Tenant for any loss or damage which may result to its stock or business by reason of such repairs, unless caused by the gross negligence or willful misconduct of Landlord, its employees, agents or contractors. Tenant shall pay to Landlord upon demand as Rent hereunder, the cost of such repairs plus interest at the Default Rate, such interest to accrue continuously from the date of payment by Landlord until repayment by Tenant. Notwithstanding the foregoing, Landlord shall have the right to make such repairs without notice to Tenant in the event of an emergency, or if such repairs relate to the exterior of the Premises. At the expiration of this Lease, Tenant shall surrender the Premises in good condition, excepting reasonable wear and tear and casualties not required to be repaired by Tenant. If Landlord elects to store any personal property of Tenant, including goods, wares, merchandise, inventory, trade fixtures and other personal property of Tenant, same shall be stored at the sole risk of Tenant. Unless caused by the gross negligence or willful misconduct of Landlord, its employees, agents or contractors, Landlord and its agents shall not be liable for any loss or damage to persons or property resulting from fire, explosion, falling plaster, steam, gas, electricity, water or rain which may leak from any part of the Complex or from the pipes, appliances or plumbing works therein or from the roof, street or subsurface or from any other places resulting from dampness or any other cause whatsoever, or from the act or negligence of any other tenant or any officer, agent, employee, contractor or guest of any such tenant. It is generally understood that mold spores are present essentially everywhere and that mold can grow in most any moist location. Emphasis is properly placed on prevention of moisture and on good housekeeping and ventilation practices. Tenant acknowledges the necessity of housekeeping, ventilation, and moisture control (especially in kitchens, janitor's closets, bathrooms, break rooms and around outside walls) for mold prevention. In signing this Lease, Tenant has first inspected the Premises and certifies that it has not observed mold, mildew or moisture within the Premises. Tenant agrees to promptly notify Landlord if it observes mold/mildew and/or moisture conditions (from any source, including leaks), and allow Landlord to evaluate and make recommendations and/or take appropriate corrective action. **TENANT RELIEVES LANDLORD FROM ANY LIABILITY FOR ANY BODILY INJURY OR DAMAGES TO PROPERTY CAUSED BY OR ASSOCIATED WITH MOISTURE OR THE GROWTH OF OR OCCURRENCE OF MOLD OR MILDEW ON THE PREMISES, UNLESS SAME IS IN EXISTENCE ON THE DATE OF THIS LEASE OR IS CAUSED BY THE GROSS NEGLIGENCE OR WILLFUL MISCONDUCT OF LANDLORD, ITS EMPLOYEES, AGENTS OR CONTRACTORS.** In addition, execution of this Lease constitutes acknowledgement by Tenant that control of moisture and mold prevention are integral to its Lease obligations.

Notwithstanding Tenant's repair and maintenance obligations pursuant to this Section 8(b)(ii), if any item of Tenant's repair and maintenance obligations set forth herein involves a capital repair, replacement, improvement and/or equipment under generally accepted accounting principles consistently applied ("**Tenant Repair Capital Item**"), Tenant shall provide written notice thereof to Landlord. Landlord shall, pursuant to the receipt of such notice from Tenant, make such Tenant Repair Capital Item, and following completion thereof, provide Tenant with written notice of (i) the total cost of such Tenant Repair Capital Item ("**Tenant Repair Capital Item Cost**"), (ii) the estimated useful life of such Tenant Repair Capital Item per generally accepted accounting principles consistently applied ("**Useful Life**"), (iii) the amortization of such Tenant Repair Capital Item Cost over such Useful Life at an interest rate equal to the "prime rate" as announced from time to time by Bank of America, N.A., plus one percent (1%) per annum, and (iv) the monthly amount due and payable by Tenant to reimburse Landlord for that portion of the amortized Tenant Repair Capital Item Cost applicable to the remainder of the Lease Term, which monthly amount shall be paid by Tenant to Landlord concurrently with the payment by Tenant to Landlord of the monthly Base Rent.

(iii) **Performance of Work.** All work described in this Section 8 shall be performed only by contractors and subcontractors approved in writing by Landlord, which approval shall not be unreasonably withheld, conditioned or delayed. Tenant shall cause all contractors and subcontractors to procure and maintain insurance coverage naming Landlord and Landlord's property management company as additional insureds against such risks, in such amounts, on such forms, and with such companies as Landlord may reasonably require as set forth on Exhibit I attached hereto. Tenant shall provide Landlord with the identities, mailing addresses and telephone numbers of all contractors and subcontractors performing work or supplying materials prior to beginning such construction and Landlord may post on and about the Premises notices of non-responsibility pursuant to applicable Laws. All such work shall be performed in accordance with all Laws and in a good and workmanlike manner so as not to damage the Building (including the Premises, the Building's Structure and the Building's Systems). All such work which may affect the Building's Structure or the Building's Systems, at Landlord's election, must be performed by Landlord's usual contractor for such work or a contractor approved by Landlord, which approval shall not be unreasonably withheld, conditioned or delayed. All work affecting the roof of the Building must be performed by Landlord's roofing contractor or a contractor approved by Landlord, which approval shall

not be unreasonably withheld, conditioned or delayed, and no such work will be permitted if it would void or reduce the warranty on the roof. All work by Tenant shall conform, at a minimum, to the Building Standards attached hereto as Exhibit K, as the same may be modified by Landlord from time to time.

(c) **Mechanic's Liens.** All work performed, materials furnished, or obligations incurred by or at the request of a Tenant Party shall be deemed authorized and ordered by Tenant only, and Tenant shall not permit any mechanic's liens to be filed against the Premises or the Project in connection therewith. Upon completion of any such work, Tenant shall deliver to Landlord final lien waivers from all contractors, subcontractors and materialmen who performed such work. If such a lien is filed, then Tenant shall, within thirty (30) days (unless Landlord is in the process of selling the Building or obtaining financing, in which case Tenant shall within ten (10) days) after Landlord has delivered notice of the filing thereof to Tenant (or such earlier time period as may be necessary to prevent the forfeiture of the Premises, Project or any interest of Landlord therein or the imposition of a civil or criminal fine with respect thereto), either: (1) pay the amount of the lien and cause the lien to be released of record; or (2) diligently contest such lien and deliver to Landlord a bond or other security reasonably satisfactory to Landlord. If Tenant fails to timely take either such action, then Landlord may pay the lien claim, and any amounts so paid, including expenses and interest, shall be paid by Tenant to Landlord within thirty (30) days after Landlord has invoiced Tenant therefor. Landlord and Tenant acknowledge and agree that their relationship is and shall be solely that of "landlord-tenant" (thereby excluding a relationship of "owner-contractor," "owner-agent" or other similar relationships). Accordingly, all materialmen, contractors, artisans, mechanics, laborers and any other persons now or hereafter contracting with Tenant, any contractor or subcontractor of Tenant or any other Tenant Party for the furnishing of any labor, services, materials, supplies or equipment with respect to any portion of the Premises, at any time from the date hereof until the end of the Term, are hereby charged with notice that they look exclusively to Tenant to obtain payment for same. Nothing herein shall be deemed a consent by Landlord to any liens being placed upon the Premises, Project or Landlord's interest therein due to any work performed by or for Tenant or deemed to give any contractor or subcontractor or materialman any right or interest in any funds held by Landlord to reimburse Tenant for any portion of the cost of such work. **TENANT SHALL INDEMNIFY, DEFEND AND HOLD HARMLESS LANDLORD, ITS PROPERTY MANAGER, ANY SUBSIDIARY OR AFFILIATE OF THE FOREGOING, AND THEIR RESPECTIVE OFFICERS, DIRECTORS, SHAREHOLDERS, PARTNERS, EMPLOYEES, MANAGERS, CONTRACTORS, ATTORNEYS AND AGENTS (COLLECTIVELY, THE "INDEMNITEES") FROM AND AGAINST ALL CLAIMS, DEMANDS, CAUSES OF ACTION, SUITS, JUDGMENTS, DAMAGES AND EXPENSES (INCLUDING REASONABLE ATTORNEYS' FEES) IN ANY WAY ARISING FROM OR RELATING TO THE FAILURE BY ANY TENANT PARTY TO PAY FOR ANY WORK PERFORMED, MATERIALS FURNISHED, OR OBLIGATIONS INCURRED BY OR AT THE REQUEST OF A TENANT PARTY.** The foregoing indemnity shall survive termination or expiration of this Lease.

(d) **Signs.**

(i) **General Signs.** Tenant shall not place or permit to be placed any signs upon: (i) the roof of the Premises; or (ii) the Common Areas; or (iii) any exterior area of the Building without Landlord's prior written approval, which approval shall not be unreasonably withheld, conditioned or delayed provided any proposed sign is placed only in those locations as may be designated by Landlord, and complies with the sign criteria promulgated by Landlord from time to time and applicable Law. Upon request of Landlord, Tenant shall promptly remove any sign or other materials which Tenant has placed or permitted to be placed upon the exterior or interior surface of any door or window inside the Premises, or the exterior of the Building, if: (i) required in connection with any cleaning, maintenance or repairs to the Building; or (ii) placed without Landlord's prior written approval as set forth above. If Tenant fails to do so, Landlord may without liability unless caused by the gross negligence or willful misconduct of Landlord, its employees, agents or contractors, remove the same at Tenant's expense. Tenant shall comply with such regulations as may from time to time be promulgated by Landlord governing signs, advertising material or lettering of all tenants in the Project or Complex, as applicable. Tenant shall be responsible for the repair, painting or replacement of the Building fascia surface or other portion of the Building where signs are attached, upon vacation of the Premises, or the removal or alteration of its sign for any reason. If Tenant fails to do so, Landlord may have the sign removed and the cost of removal shall be payable by Tenant within thirty (30) days of invoice.

(ii) **Building Top Signs.** Subject to the terms of this Section 8 and applicable laws, Landlord hereby grants Tenant and Tenant's Permitted Transferee (as hereinafter defined in Section 10(f)) the exclusive right, at Tenant's sole cost and expense and as long as Tenant fulfills the Occupancy Requirement (as hereinafter defined), to install the maximum building top signage allowed under applicable Law at a location or locations reasonably approved by Landlord (which may include both Tenant's name, which shall be restricted to only Ultragenyx and corporate logo) ("**Building Top Sign**").

Tenant's Building Top Sign shall be subject to all applicable Law and the sign criteria promulgated by Landlord from time to time. The content, size, design, graphics, materials, colors and other specifications of the Building Top Sign (including without limitation, the exact location of any and all of the Building Top Sign), and all contractors or subcontractors utilized by Tenant in connection therewith, shall be subject to the approval of Landlord, which shall not be unreasonably withheld, conditioned

or delayed, and shall be consistent with the exterior design, materials and appearance of the Building and the signage program of the Building, if any. Tenant shall be responsible for all costs and expenses incurred in connection with the design, construction, installation, repair, operation, maintenance, compliance with laws, utilities (including the costs of metering such utilities usage and the cost of the meter) and removal of the Building Top Sign. Tenant shall also be responsible for the cost of all utilities (if any) utilized in connection with the Building Top Sign. Should the name of Tenant be changed to another name (the “**New Name**”), Tenant shall be entitled to modify, at Tenant’s sole cost and expense, Tenant’s name on the Building Top Sign to reflect Tenant’s New Name, so long as (a) the New Name is not an “**Objectionable Name**”, (b) Landlord shall have granted its consent to such New Name (which consent shall not be unreasonably withheld), (c) Tenant’s New Name shall be subject to the then existing signage rights of any tenant or occupant within the Complex, and (d) Tenant’s New Name shall not cause Landlord to be in violation of an exclusivity granted to another tenant at the Complex. The term “**Objectionable Name**” shall mean any name which relates to an entity which is of a character or reputation, or is associated with a political orientation or faction, which is inconsistent with the quality of the Complex, or which would otherwise reasonably offend a landlord of buildings comparable to and in the vicinity of the Building. In addition, Tenant’s right to maintain any of the Building Top Sign shall terminate at any time during the Lease Term during which the Occupancy Requirement is no longer satisfied or an Event of Default by Tenant has occurred under this Lease. Upon the expiration of the Lease Term or the earlier termination of Tenant’s signage rights under this Section 8(d)(ii), Tenant shall, at Tenant’s sole cost and expense, remove the Building Top Sign and repair any and all damage to the Building caused by such removal.

For purposes of this Section 8(d)(ii), “**Occupancy Requirements**” shall mean that Tenant or Tenant’s Permitted Transferee is leasing and physically occupying at a minimum fifty percent (50%) of the Premises and no Event of Default by Tenant has occurred under this Lease.

#### 9. **Use; Compliance with Laws.**

(a) **Use.** Tenant shall continuously occupy and use the Premises only for the Permitted Use (as set forth in the Basic Lease Information) and shall comply with all Laws relating to the use, condition, access to, and occupancy of the Premises and will not commit waste, overload the Building’s Structure or the Building’s Systems or subject the Premises to any use that would damage the Premises. Tenant, at its sole cost and expense, shall obtain and keep in effect during the Term, all permits, licenses, and other authorizations necessary to permit Tenant to use and occupy the Premises for the Permitted Use in accordance with applicable Laws. Notwithstanding anything in this Lease to the contrary but subject to the provisions of Section 9(b) below, as between Landlord and Tenant: (i) from and after the Delivery Date, Tenant shall bear the risk of complying with Title III of the Americans With Disabilities Act of 1990, any state laws governing handicapped access or architectural barriers, and all rules, regulations and guidelines promulgated under such laws, as amended from time to time (the “**Disabilities Acts**”) in the Premises; and (ii) Landlord shall bear the risk of complying with the Disabilities Acts in the Common Areas (subject to reimbursement as set forth in Exhibit C), other than compliance that is necessitated by the use of the Premises for other than the Permitted Use or as a result of any alterations or additions made by Tenant (which risk and responsibility shall be borne by Tenant). The Premises shall not be used for any purpose which creates strong, unusual, or offensive odors, fumes, dust or vapors; which emits noise or sounds that are objectionable due to intermittence, beat, frequency, shrillness, or loudness; which is associated with indecent or pornographic matters; or which involves political or moral issues (such as abortion issues). Tenant shall conduct its business and control each other Tenant Party so as not to create any nuisance or unreasonably interfere with other tenants or Landlord in its management of the Building. Tenant shall store all trash and garbage within the Premises or in a trash dumpster or similar container approved by Landlord as to type, location and screening; and Tenant shall arrange for the regular pick-up of such trash and garbage at Tenant’s expense (unless Landlord finds it necessary to furnish such a service, in which event Tenant shall be charged an equitable portion of the total of the charges to all tenants using the service). Receiving and delivery of goods and merchandise and removal of garbage and trash shall be made only in the manner and areas prescribed by Landlord. Tenant shall not operate an incinerator or burn trash or garbage within the Project or Complex, as applicable. Tenant shall not knowingly conduct or permit to be conducted in the Premises any activity, or place any equipment in or about the Premises or the Building, which will invalidate the insurance coverage in effect or increase the rate of fire insurance or other insurance on the Premises or the Building.

(b) **Landlord’s Compliance with Laws.** Landlord shall ensure that the Premises and the Building are in compliance with all applicable Laws, including, but not limited to the Disabilities Acts as of the Delivery Date. In the event that as of the Delivery Date (i) the Premises are not in compliance with all such federal, state and local laws and regulations, without regard to Tenant’s use of the Premises or the Tenant Improvements subsequently constructed on or installed in the Premises (herein the “**Compliance Condition**”), and (ii) Tenant delivers to Landlord written notice of the existence of the Compliance Condition (the “**Non-Compliance Notice**”) by the date which is one hundred eighty (180) days after the Commencement Date (the “**Non-Compliance Outside Date**”), then Tenant’s sole remedy shall be that Landlord shall, at Landlord’s sole cost and expense which expense shall not be included in Additional Rent, do that which is necessary to put the applicable components of the Premises and the Building described in the Non-Compliance Notice into the Compliance Condition within a reasonable period of time after Landlord’s receipt of the Non-Compliance Notice; provided, further, that to the extent any such work is required or triggered by Tenant’s proposed use of the Premises or the Tenant Improvements to be constructed therein, then Landlord shall perform such work, but Tenant shall pay Landlord for the cost of

such work within thirty (30) days after invoice by Landlord. If Tenant fails to deliver the Non-Compliance Notice to Landlord on or prior to the Non-Compliance Outside Date, Landlord shall have no obligation to perform the work described in the foregoing provisions of this Section 9(b); provided that Landlord shall remain responsible for making all alterations and improvements which are Landlord's responsibility to repair and maintain pursuant to Section 8(b)(i) above.

#### 10. Assignment and Subletting.

(a) **Transfers.** Tenant shall not, without the prior written consent of Landlord, which consent shall not unreasonably be withheld, conditioned or delayed: (1) assign, transfer, or encumber this Lease or any estate or interest herein, whether directly or by operation of law; (2) permit any other entity to become Tenant hereunder by merger, consolidation, or other reorganization; (3) if Tenant is an entity other than a corporation whose stock is publicly traded, permit the transfer of an ownership interest in Tenant so as to result in a change in the current control of Tenant; (4) sublet any portion of the Premises; (5) grant any license, concession, or other right of occupancy of any portion of the Premises; or (6) permit the use of the Premises by any parties other than Tenant (any of the events listed in Section 10(a)(1) through Section 10(a)(6) being a "Transfer").

(b) **Consent Standards.** If a proposed transferee does not meet the following conditions, Landlord shall not be deemed to have been unreasonable in withholding its consent to a Transfer (provided that the following list shall not be deemed the exclusive factors for review): (1) in the case of a Transfer that is an assignment or a sublease of the entirety of the Premises, the transferee has a Tangible Net Worth (hereinafter defined) which is not less than the lesser of (i) the Tangible Net Worth of Tenant as of the date of execution of this Lease and (ii) the Tangible Net Worth of Tenant on the date immediately prior to such assignment; (2) has a good reputation in the business community; (3) will use the Premises for the Permitted Use and will not use the Premises in any manner that would conflict with any exclusive use agreement or other similar agreement entered into by Landlord with any other tenant of the Project or Complex, as applicable; (4) will not use the Premises, Project or Complex in a manner that would materially and unreasonably increase the pedestrian or vehicular traffic to the Premises, Project or Complex; (5) is not a governmental entity, or subdivision or agency thereof; (6) is not another occupant of the Building or Complex, as applicable; (7) is not another occupant of the Building or Complex, as applicable, whose lease is scheduled to expire within three (3) years of the proposed date of the Transfer; and (8) is not a person or entity with whom Landlord is then, or has been within the three (3) month period prior to the time Tenant seeks to enter into such assignment or subletting, negotiating to lease space in the Building or Complex, as applicable, or any Affiliate of any such person or entity. In the cases of items (6) and (8) above, they shall be applicable only to the extent Landlord has comparable space in the Complex available to lease to such proposed transferee.

(c) **Request for Consent.** If Tenant requests Landlord's consent to a Transfer, then, at least thirty (30) days prior to the effective date of the proposed Transfer, Tenant shall provide Landlord with a written description of all terms and conditions of the proposed Transfer, copies of the proposed pertinent documentation, and the following information about the proposed transferee: name and address; reasonably satisfactory information about its business and business history; its proposed use of the Premises; banking, financial, and other credit information; and general references sufficient to enable Landlord to determine the proposed transferee's creditworthiness and character (collectively, the "Transfer Notice"). Concurrently with the Transfer Notice, Tenant shall pay to Landlord a fee of \$1,000 to defray Landlord's expenses in reviewing such request, and Tenant shall reimburse Landlord immediately upon request for its reasonable attorneys' fees incurred in connection with considering any request for consent to a Transfer.

(d) **Conditions to Consent.** If Landlord consents to a proposed Transfer that is an assignment of the Tenant's entire interest in the Lease, then the proposed transferee shall deliver to Landlord a written agreement whereby it expressly assumes Tenant's obligations hereunder; provided, however, any transferee of less than Tenant's entire interest in the Lease shall be liable only for the obligations under this Lease that are properly allocable to such Transfer for the period of the Transfer in which event the proposed transferee shall deliver to Landlord a written agreement whereby such sublease shall be subject and subordinate to the Lease. No Transfer shall release Tenant from its obligations under this Lease, but rather Tenant and its transferee shall be jointly and severally liable therefor. Landlord's consent to any Transfer shall not be deemed consent to any subsequent Transfers. If an Event of Default occurs while the Premises or any part thereof are subject to a Transfer, then Landlord, in addition to its other remedies, may collect directly from such transferee all rents becoming due to Tenant and apply such rents against Rent. Tenant authorizes its transferees to make payments of rent directly to Landlord upon receipt of notice from Landlord to do so following the occurrence of an Event of Default hereunder. Tenant shall pay for the cost of any demising walls or other improvements necessitated by a proposed subletting or assignment.

(e) **Attornment by Subtenants.** Each sublease by Tenant hereunder shall be subject and subordinate to this Lease and to the matters to which this Lease is or shall be subordinate, and each subtenant by entering into a sublease is deemed to have agreed that in the event of termination, re-entry or dispossession by Landlord under this Lease, Landlord may, at its option, either terminate the sublease or take over all of the right, title and interest of Tenant, as sublandlord, under such sublease, and such subtenant shall, at Landlord's option, attorn to Landlord pursuant to the then executory provisions of such sublease, except that Landlord shall not be: (1) liable for any

previous act or omission of Tenant under such sublease; (2) subject to any counterclaim, offset or defense that such subtenant might have against Tenant; (3) bound by any previous modification of such sublease or by any rent or additional rent or advance rent which such subtenant might have paid for more than the current month to Tenant, and all such rent shall remain due and owing, notwithstanding such advance payment; (4) bound by any security or advance rental deposit made by such subtenant which is not delivered or paid over to Landlord and with respect to which such subtenant shall look solely to Tenant for refund or reimbursement; or (5) obligated to perform any work in the subleased space or to prepare it for occupancy, and in connection with such attornment, the subtenant shall execute and deliver to Landlord any instruments Landlord may reasonably request to evidence and confirm such attornment. Each subtenant or licensee of Tenant shall be deemed, automatically upon and as a condition of its occupying or using the Premises or any part thereof, to have agreed to be bound by the terms and conditions set forth in this Section 10(e). The provisions of this Section 10(e) shall be self-operative, and no further instrument shall be required to give effect to this provision.

(f) **Permitted Transfers.** Notwithstanding Section 10(a), Tenant may Transfer all or part of its interest in this Lease or all or part of the Premises (a “**Permitted Transfer**”) to the following types of entities (a “**Permitted Transferee**”) without the written consent of Landlord:

(1) an Affiliate of Tenant;

(2) any corporation, limited partnership, limited liability partnership, limited liability company or other business entity in which or with which Tenant, or its corporate successors or assigns, is merged or consolidated, in accordance with applicable statutory provisions governing merger and consolidation of business entities, so long as (A) Tenant’s obligations hereunder are assumed by the entity surviving such merger or created by such consolidation; and (B) the Tangible Net Worth of the surviving or created entity is not less than the lesser of (i) the Tangible Net Worth of Tenant as of the date of execution of this Lease and (ii) the Tangible Net Worth of Tenant on the date immediately prior to such Permitted Transfer; or

(3) any corporation, limited partnership, limited liability partnership, limited liability company or other business entity acquiring all or substantially all of Tenant’s assets if such entity’s Tangible Net Worth after such acquisition is not less than the lesser of (i) the Tangible Net Worth of Tenant as of the date of execution of this Lease and (ii) the Tangible Net Worth of Tenant on the date immediately prior to such Permitted Transfer.

Tenant shall promptly notify Landlord of any such Permitted Transfer. Tenant shall remain liable for the performance of all of the obligations of Tenant hereunder, or if Tenant no longer exists because of a merger, consolidation, or acquisition, the surviving or acquiring entity shall expressly assume in writing the obligations of Tenant hereunder. Additionally, the Permitted Transferee shall comply with all of the terms and conditions of this Lease, including the Permitted Use, and the use of the Premises by the Permitted Transferee may not violate any other agreements affecting the Premises, the Building or the Complex, Landlord or other tenants of the Complex. No later than five (5) Business Days after the effective date of any Permitted Transfer, Tenant agrees to furnish Landlord with (A) copies of the instrument effecting any of the foregoing Transfers, (B) documentation establishing Tenant’s satisfaction of the requirements set forth above applicable to any such Transfer, and (C) evidence of insurance as required under this Lease with respect to the Permitted Transferee. The occurrence of a Permitted Transfer shall not waive Landlord’s rights as to any subsequent Transfers. “**Tangible Net Worth**” means the excess of total assets over total liabilities, in each case as determined in accordance with generally accepted accounting principles consistently applied (“**GAAP**”), excluding, however, from the determination of total assets all assets which would be classified as intangible assets under GAAP including goodwill, licenses, patents, trademarks, trade names, copyrights, and franchises. Any subsequent Transfer by a Permitted Transferee shall be subject to the terms of this Section 10.

(g) **Additional Compensation.** Tenant shall pay to Landlord, immediately upon receipt thereof, fifty percent (50%) of the excess of all compensation received by Tenant for a Transfer over the Rent allocable to the portion of the Premises covered thereby, after deducting the following costs and expenses for such Transfer (which costs will be amortized over the term of the sublease or assignment pursuant to sound accounting principles and deducted monthly from such excess): (1) brokerage commissions and reasonable attorneys’ fees; (2) advertising for subtenants or assignees; (3) the actual costs paid in making any improvements or substitutions in the Premises required by any sublease or assignment; and (4) the costs of any inducements or concessions given to the subtenant or assignee.

(h) **Landlord’s Option.** Notwithstanding anything to the contrary contained in this Article 10, Landlord shall have the option, by giving written notice to Tenant within thirty (30) days after receipt of any Transfer Notice with respect to (i) a proposed assignment of this Lease by Tenant, or (ii) a proposed sublease of at least any one floor of the Premises (the portion of the Premises proposed to be transferred pursuant to clause (i) or (ii), the “**Subject Space**”) to (x) recapture the Subject Space, or (y) take an assignment or sublease of the Subject Space from Tenant. Such recapture, or sublease or assignment notice shall cancel and terminate this Lease, or create a sublease or assignment, as the case may be, with respect to the Subject Space as of the date stated in the Transfer Notice as the effective date of the proposed Transfer until the last day of the term of the Transfer as set forth in the Transfer Notice. In the event of a recapture by Landlord, if this Lease shall be canceled with respect to less than the entire Premises, the Rent

reserved herein shall be prorated on the basis of the number of square feet retained by Tenant in proportion to the number of square feet contained in the Premises, and this Lease as so amended shall continue thereafter in full force and effect, and upon request of either party, the parties shall execute written confirmation of the same. In the event of a recapture by Landlord of Subject Space that contains less than a full floor of the Premises, Tenant shall be responsible, at its sole cost and expense, for demising the Premises as necessary, including, without limitation, the construction of a common corridor and demising walls, and the separation of electrical, plumbing, mechanical, HVAC, life-safety and other Building services, systems and utilities on the subject floor(s), all in accordance with the terms of this Lease, including without limitation, Section 8 hereof. If Landlord declines, or fails to elect in a timely manner to recapture, sublease or take an assignment of the Subject Space under this Section 10(h), then, provided Landlord has consented to the proposed Transfer, Tenant shall be entitled to proceed to transfer the Subject Space to the proposed Transferee, subject to provisions of this Section 10.

11. **Insurance; Waivers; Subrogation; Indemnity.**

(a) **Indemnity Agreement.** TO THE FULLEST EXTENT PERMITTED BY LAW, TENANT WILL DEFEND, INDEMNIFY AND HOLD LANDLORD HARMLESS FROM AND AGAINST ALL CLAIMS (AS DEFINED HEREIN) ARISING OUT OF OR RELATING (DIRECTLY OR INDIRECTLY) TO (I) THE CONDUCT OR MANAGEMENT OF THE PREMISES OR OF ANY BUSINESS THEREIN, OR ANY WORK OR THING WHATSOEVER DONE, OR ANY CONDITION CREATING IN OR ABOUT THE PREMISES DURING THE TERM; (II) ANY ACT, OMISSION, BREACH OF ANY PROVISION OF THIS LEASE, OR NEGLIGENCE OF TENANT OR ANY OF TENANT'S LICENSEES OR THE PARTNERS, DIRECTORS, OFFICERS, AGENTS, EMPLOYEES, INVITEES OR CONTRACTORS OF TENANT OR ANY OF TENANT'S LICENSEES; AND (III) ANY ACCIDENT, INJURY OR DAMAGE WHATSOEVER OCCURRING IN OR AT THE PREMISES. TENANT HEREBY EXPRESSLY INDEMNIFIES LANDLORD FOR THE CONSEQUENCES OF ANY NEGLIGENT ACT OF OMISSION OF LANDLORD, ITS AGENTS, SERVANTS AND EMPLOYEES, UNLESS THE CLAIM IS CAUSED BY THE SOLE NEGLIGENCE OF LANDLORD.

(b) **Tenant's Insurance.** Effective as of the Delivery Date and continuing throughout the Term, Tenant shall maintain insurance of the types and in the amounts described below. Insurance shall be obtained from insurance carriers rated not less than A-VIII by A.M. Best Company and licensed to business in the State. Tenant insurance policy deductibles shall be the responsibility of the Tenant and shall be less than \$25,000 unless approved by Landlord. Tenant's insurance policies shall be primary and not require any contribution by any insurance maintained by Landlord. If Tenant fails to comply with the foregoing insurance requirements or to deliver to Landlord the certificates or evidence of coverage required herein, Landlord, in addition to any other remedy available pursuant to this Lease or otherwise, may, but shall not be obligated to, obtain such insurance and Tenant shall pay to Landlord on demand the premium costs thereof, plus an administrative fee of fifteen percent (15%) of such cost. It is expressly understood and agreed that the foregoing minimum limits of insurance coverage shall not limit the liability of Tenant for its acts or omissions as provided in this Lease. Failure of Landlord to demand such certificate or other evidence of full compliance with these insurance requirements or failure of Landlord to identify a deficiency from evidence that is provided shall not be construed as a waiver of Tenant's obligation to maintain such insurance. These requirements and limits are subject to review and modification by the Landlord in recognition of changes in the occupancy, exposure, or insurance marketplace.

(i) **Commercial General Liability Insurance** written on an occurrence basis, using a form that is at least as broad as ISO commercial general liability form (CG 00 01) and shall cover liability arising from premises, operations, independent contractors, products-completed operations, personal injury and advertising injury, and liability assumed under an insured contract naming the Landlord and Landlord's property management company as named insureds with limits of not less than \$1,000,000 each occurrence and \$2,000,000 aggregate per location shall be maintained. Evidence of commercial general liability insurance granting no less than thirty (30) days' notice of cancellation for reasons other than non-payment shall be provided by the ISO form (CG 20 11, CG 20 26 11 85, or a substitute providing equivalent coverage and under the commercial umbrella policy) prior to Lease inception and no less than fifteen (15) days prior to each insurance policy renewal during the term of the Lease.

(ii) **Commercial Auto Liability Insurance**, if the Tenant owns any automobiles, written on a coverage form that is at least as broad as the ISO business auto coverage form (CA 00 01) to cover owned, non-owned, hired, and borrowed autos with not less than \$1,000,000 combined single limit shall be obtained. If the Tenant does not own any vehicles, non-owned and hired auto liability insurance with a not less than \$1,000,000 limit shall be maintained. Tenant shall require similar coverage for any contract vehicles that it engages for transportation of personnel or personal property to or from the Premises.

(iii) **Workers Compensation Insurance** in accordance with statutory requirements.

(iv) **Employers' Liability Insurance** with limits not less than \$1,000,000 per accident shall be maintained.

(v) **Umbrella or Excess Liability Insurance** over (i), (ii), and (iv) with limits of not less than \$4,000,000 each occurrence and \$4,000,000 aggregate.

(vi) Intentionally omitted.

(vii) **Commercial Property Insurance** with a limit equal to the full replacement cost and covering the fixtures, personal property, equipment, tenant improvements and betterments that will, at a minimum, cover the perils insured under ISO special causes of loss form (CP 10 30) and broad causes of loss form (CP 10 20) or their equivalent shall be provided.

(viii) If required by Landlord due to the nature of tenant's operation, **Boiler & Machinery Insurance** covering the fixtures, personal property, equipment, tenant improvements and betterments from loss or damage caused by machinery breakdown or the explosion of steam boilers or pipes.

(ix) If required by Landlord due to the nature of tenant's operation, **Boiler & Machinery Insurance** covering the fixtures, personal property, equipment, tenant improvements and betterments from loss or damage caused by machinery breakdown or the explosion of steam boilers or pipes.

(x) **Business Income insurance** with a limit adequate to pay for one year's loss of business income resulting from suspension of the Tenant's business operations, caused by property damage from a covered cause of loss to the Premises.

(c) **Landlord's Insurance**. Throughout the Term of this Lease, Landlord shall maintain, as a minimum, the following insurance policies. Tenant shall pay its Proportionate Share of the cost of all insurance carried by Landlord with respect to the Project or Complex, as set forth in **Exhibit C**. Landlord's insurance policies shall be for the sole benefit of Landlord and under Landlord's sole control, and Tenant shall have no right or claim to any proceeds thereof or any other rights thereunder:

(i) **Building Insurance** with a limit equal to full replacement cost less a commercially-reasonable deductible if the Landlord so chooses.

(ii) **Commercial General Liability and Umbrella Insurance** in an amount not less than \$5,000,000.

(iii) **Other insurance** and additional coverage as Landlord may deem necessary.

(d) **No Subrogation**. LANDLORD AND TENANT EACH WAIVES ANY CLAIM IT MIGHT HAVE AGAINST THE OTHER FOR ANY DAMAGE TO OR THEFT, DESTRUCTION, LOSS, OR LOSS OF USE OF ANY PROPERTY, TO THE EXTENT THE SAME IS INSURED AGAINST UNDER ANY INSURANCE POLICY THAT COVERS THE BUILDING, THE PREMISES, LANDLORD'S OR TENANT'S FIXTURES, PERSONAL PROPERTY, LEASEHOLD IMPROVEMENTS, OR BUSINESS, OR IS REQUIRED TO BE INSURED AGAINST UNDER THE TERMS HEREOF, REGARDLESS OF WHETHER THE NEGLIGENCE OF THE OTHER PARTY CAUSED SUCH LOSS. LANDLORD AND TENANT EACH HEREBY WAIVE ANY RIGHT OF SUBROGATION AND RIGHT OF RECOVERY OR CAUSE OF ACTION FOR INJURY INCLUDING DEATH OR DISEASE TO RESPECTIVE EMPLOYEES OF EITHER AS COVERED BY WORKER'S COMPENSATION (OR WHICH WOULD HAVE BEEN COVERED IF TENANT OR LANDLORD AS THE CASE MAY BE, WAS CARRYING THE INSURANCE AS REQUIRED BY THIS LEASE). EACH PARTY SHALL CAUSE ITS INSURANCE CARRIER TO ENDORSE ALL APPLICABLE POLICIES WAIVING THE CARRIER'S RIGHTS OF RECOVERY UNDER SUBROGATION OR OTHERWISE AGAINST THE OTHER PARTY.

#### 12. **Subordination; Attornment; Notice to Landlord's Mortgagee.**

(a) **Subordination**. This Lease shall be subordinate to any deed of trust, mortgage, or other security instrument (each, a "**Mortgage**"), or any ground lease, master lease, or primary lease (each, a "**Primary Lease**"), that now or hereafter covers all or any part of the Premises (the mortgagee under any such Mortgage, beneficiary under any such deed of trust, or the lessor under any such Primary Lease is referred to herein as a "**Landlord's Mortgagee**"). Any Landlord's Mortgagee may elect at any time, unilaterally, to make this Lease superior to its Mortgage, Primary Lease, or other interest in the Premises by so notifying Tenant in writing. The provisions of this Section shall be self-operative and no further instrument of subordination shall be required; however, in confirmation of such subordination, Tenant shall execute and return to Landlord (or such other party designated by Landlord) within ten (10) days after written request therefor such documentation, in recordable form if required, as a Landlord's Mortgagee may reasonably request to evidence the subordination of this Lease to such Landlord's Mortgagee's Mortgage or Primary Lease (including a subordination, non-disturbance and attornment agreement) or, if the Landlord's Mortgagee so elects, the subordination of such Landlord's Mortgagee's Mortgage or Primary Lease to this Lease. Notwithstanding the foregoing, Tenant shall not be obligated to execute any document which alters any material provision of the Lease.

Landlord shall use its commercially reasonable efforts to provide Tenant with a commercially reasonable non-disturbance, subordination and attornment agreement in favor of Tenant from any mortgage holder in existence as of the date of this Lease (“**Superior Mortgagee**”). Landlord agrees to provide Tenant with commercially reasonable non-disturbance, subordination and attornment agreement(s) in favor of Tenant from any Superior Mortgagee(s) of Landlord who later come(s) into existence at any time prior to the expiration of the Term of the Lease in consideration of, and as a condition precedent to, Tenant’s agreement to be bound by this Section 12(a).

(b) **Attornment.** Tenant shall attorn to any party succeeding to Landlord’s interest in the Premises, whether by purchase, foreclosure, deed in lieu of foreclosure, power of sale, termination of lease, or otherwise, upon such party’s request, and shall execute such agreements confirming such attornment as such party may reasonably request. Notwithstanding the foregoing, Tenant shall not be obligated to execute any document which alters any material provision of the Lease.

(c) **Notice to Landlord’s Mortgagee.** Tenant shall not seek to enforce any remedy it may have for any default on the part of Landlord without first giving written notice by certified mail, return receipt requested, specifying the default in reasonable detail, to any Landlord’s Mortgagee whose address has been given to Tenant, and affording such Landlord’s Mortgagee a reasonable opportunity to perform Landlord’s obligations hereunder.

13. **Rules and Regulations.** Tenant shall comply with the rules and regulations of the Building which are attached hereto as Exhibit E. Landlord may, from time to time, change such rules and regulations for the safety, care, or cleanliness of the Building and related facilities, provided that such changes are applicable to all tenants of the Building, will not unreasonably interfere with Tenant’s use of the Premises, will not modify any of the provisions of the Lease, and are enforced by Landlord in a non-discriminatory manner. Tenant shall be responsible for the compliance with such rules and regulations by each Tenant Party.

#### 14. **Condemnation.**

(a) **Total Taking.** If the entire Building or Premises are taken by right of eminent domain or conveyed in lieu thereof (a “**Taking**”), this Lease shall terminate as of the date of the Taking.

(b) **Partial Taking - Tenant’s Rights.** If any part of the Building becomes subject to a Taking and such Taking will prevent Tenant from conducting its business in the Premises in a manner reasonably comparable to that conducted immediately before such Taking for a period of more than one hundred eighty (180) days, then Tenant may terminate this Lease as of the date of such Taking by giving written notice to Landlord within thirty (30) days after the Taking, and Rent shall be apportioned as of the date of such Taking. If Tenant does not terminate this Lease, then Rent shall be abated on a reasonable basis as to that portion of the Premises rendered untenable by the Taking. **TENANT HEREBY WAIVES ANY AND ALL RIGHTS IT MIGHT OTHERWISE HAVE PURSUANT TO SECTION 1265.130 OF THE CALIFORNIA CODE OF CIVIL PROCEDURE.**

(c) **Partial Taking - Landlord’s Rights.** If any material portion, but less than all, of the Building becomes subject to a Taking, or if Landlord is required to pay any of the proceeds arising from a Taking to a Landlord’s Mortgagee, then Landlord may terminate this Lease by delivering written notice thereof to Tenant within thirty (30) days after such Taking, and Rent shall be apportioned as of the date of such Taking. If Landlord does not so terminate this Lease, then this Lease will continue, but if any portion of the Premises has been taken, Rent shall abate as provided in the next to last sentence of Section 14(b).

(d) **Award.** If any Taking occurs, then Landlord shall receive the entire award or other compensation for the Land, the Building, and other improvements taken; however, Tenant may separately pursue a claim (to the extent it will not reduce Landlord’s award) against the condemnor for the value of Tenant’s personal property which Tenant is entitled to remove under this Lease, moving costs, loss of business and goodwill, and other claims it may have (excluding any claim related to its leasehold interest).

(e) **Repair.** If the Lease is not terminated, Landlord shall proceed with reasonable diligence to restore the remaining part of the Premises and Building substantially to their former condition to the extent feasible to constitute a complete and tenantable Building and Premises; provided, however, that Landlord shall only be required to reconstruct building standard leasehold improvements existing in the Premises as of the date of the Taking, and Tenant shall be required to pay the cost for restoring any other leasehold improvements. In no event shall Landlord be required to spend more than the condemnation proceeds received by Landlord for such repair.

#### 15. **Fire or Other Casualty.**

(a) **Repair Estimate.** If the Premises or the Building are damaged by fire or other casualty (a “**Casualty**”), Landlord shall use good faith efforts to deliver to Tenant within sixty (60) days after such Casualty a good faith estimate (the “**Damage Notice**”) of the time needed to repair the damage caused by such Casualty.

(b) **Tenant's Rights.** If a material portion of the Premises is damaged by Casualty such that Tenant is prevented from conducting its business in the Premises in a manner reasonably comparable to that conducted immediately before such Casualty and Landlord estimates that the damage caused thereby cannot be repaired within three hundred sixty-five (365) days after the date of the casualty (the "**Repair Period**"), then Tenant may terminate this Lease by delivering written notice to Landlord of its election to terminate within thirty (30) days after the Damage Notice has been delivered to Tenant.

(c) **Landlord's Rights.** If a Casualty damages the Premises or a material portion of the Building and: (1) Landlord estimates that the damage to the Premises cannot be repaired within the Repair Period; (2) the damage to the Premises exceeds fifty percent (50%) of the replacement cost thereof (excluding foundations and footings), as estimated by Landlord, and such damage occurs during the last two (2) years of the Term (unless Tenant exercises any renewal rights it may have in the Lease); (3) regardless of the extent of damage to the Premises, Landlord makes a good faith determination that restoring the Building would be uneconomical; or (4) Landlord is required to pay any insurance proceeds arising out of the Casualty to a Landlord's Mortgagee, then Landlord may terminate this Lease by giving written notice of its election to terminate within thirty (30) days after the Damage Notice has been delivered to Tenant.

(d) **Repair Obligation.** If neither party elects to terminate this Lease following a Casualty, then Landlord shall, within a reasonable time after such Casualty, begin to repair the Premises and shall proceed with reasonable diligence to restore the Premises to substantially the same condition as they existed immediately before such Casualty; however, other than building standard leasehold improvements Landlord shall not be required to repair or replace any Alterations or betterments within the Premises (which shall be promptly and with due diligence repaired and restored by Tenant at Tenant's sole cost and expense) or any furniture, equipment, trade fixtures or personal property of Tenant or others in the Premises or the Building. If Landlord fails to complete repairs to the Premises within three hundred sixty-five (365) days after the date of the casualty, subject to force majeure delays, then Tenant shall have the right to terminate the Lease upon written notice delivered to Landlord at any time after such three hundred sixty-five (365) day period and prior to Landlord's Substantial Completion of such repairs. If this Lease is terminated under the provisions of this Section 15, Landlord shall be entitled to the full proceeds of the insurance policies providing coverage for all Alterations, improvements and betterments in the Premises (and, if Tenant has failed to maintain insurance on such items as required by this Lease, Tenant shall pay Landlord an amount equal to the proceeds Landlord would have received had Tenant maintained insurance on such items as required by this Lease).

(e) **Abatement of Rent.** If the Premises are damaged by Casualty, Rent for the portion of the Premises rendered untenable by the damage shall be abated on a reasonable basis from the date of damage until the completion of Landlord's repairs (or until the date of termination of this Lease by Landlord or Tenant as provided above, as the case may be).

(f) **Waiver of Statutory Provisions.** The provisions of this Lease, including this Section 15, constitute an express agreement between Landlord and Tenant with respect to any and all damage to, or destruction of, all or any part of the Premises, the Building or any other portion of the Project, and any statute or regulation of the State of California, including, without limitation, Sections 1932(2) and 1933(4) of the California Civil Code, with respect to any rights or obligations concerning damage or destruction in the absence of an express agreement between the parties, and any other statute or regulation, now or hereafter in effect, shall have no application to this Lease or any damage or destruction to all or any part of the Premises, the Building or any other portion of the Project.

16. **Personal Property Taxes.** Tenant shall be liable for all taxes levied or assessed against personal property, furniture, or fixtures placed by Tenant in the Premises or in or on the Building or Project. If any taxes for which Tenant is liable are levied or assessed against Landlord or Landlord's property and Landlord elects to pay the same, or if the assessed value of Landlord's property is increased by inclusion of such personal property, furniture or fixtures and Landlord elects to pay the taxes based on such increase, then Tenant shall pay to Landlord, within thirty (30) days following written request therefor, the part of such taxes for which Tenant is primarily liable hereunder.

17. **Events of Default.** Each of the following occurrences shall be an "**Event of Default**":

(a) **Payment Default.** Tenant's failure to pay Rent within five (5) calendar days after Tenant's receipt of Landlord's written notice that the same is due; provided, however, Landlord shall not be obligated to provide written notice of monetary default more than twice in any calendar year, and each subsequent monetary default shall be an Event of Default if not received within five (5) days after the same is due;

(b) **Abandonment.** Tenant abandons the Premises or any substantial portion thereof, or fails to continuously operate its business in the Premises, abandonment being defined as Tenant's vacation of the Premises and failure to meet one (1) or more lease obligations, and such conditioned is not remedied within ten (10) days after written notice to Tenant;

(c) **Estoppel/Financial Statement/Commencement Date Letter.** Tenant fails to provide: (i) any estoppel certificate after Landlord's written request therefor pursuant to Section 26(e); (ii) any financial statement after Landlord's written request therefor pursuant to Section 26(q); or (iii) the Confirmation of Commencement Date in the form of Exhibit F as required by Section 3, and such failure shall continue for five (5) calendar days after Landlord's second (2<sup>nd</sup>) written notice thereof to Tenant;

(d) **Insurance.** Tenant fails, within five (5) calendar days following written notice from Landlord, to procure, maintain and deliver to Landlord evidence of the insurance policies and coverages as required under Section 11(b);

(e) **Mechanic's Liens.** Tenant fails to pay and release of record, or diligently contest and bond around, any mechanic's lien filed against the Premises or the Project for any work performed, materials furnished, or obligation incurred by or at the request of Tenant, within the time and in the manner required by Section 8(c);

(f) **Other Defaults.** Tenant's failure to perform, comply with, or observe any other agreement or obligation of Tenant under this Lease and the continuance of such failure for a period of thirty (30) calendar days or more after Landlord has delivered to Tenant written notice thereof; provided, however, if such default is of the type which cannot reasonably be cured within thirty (30) days, then Tenant shall have such longer time as is reasonably necessary provided Tenant commences to cure within ten (10) days after receipt of written notice from Landlord and diligently prosecutes such cure to completion within sixty (60) days of such notice; and

(g) **Insolvency.** The filing of a petition by or against Tenant (the term "Tenant" shall include, for the purpose of this Section 17(g), any guarantor of Tenant's obligations hereunder): (1) in any bankruptcy or other insolvency proceeding; (2) seeking any relief under any state or federal debtor relief law; (3) for the appointment of a liquidator or receiver for all or substantially all of Tenant's property or for Tenant's interest in this Lease; or (4) for the reorganization or modification of Tenant's capital structure; however, if such a petition is filed against Tenant, then such filing shall not be an Event of Default unless Tenant fails to have the proceedings initiated by such petition dismissed within ninety (90) calendar days after the filing thereof.

**18. Remedies.** Upon an Event of Default, Landlord shall have, in addition to any other remedies available to Landlord at law or in equity, the option to pursue any one or more of the following remedies, each and all of which shall be cumulative and nonexclusive, without any notice or demand whatsoever.

(a) Terminate this Lease, in which event Tenant shall immediately surrender the Premises to Landlord, and if Tenant fails to do so, Landlord may, without prejudice to any other remedy which it may have for possession or arrearages in rent, enter upon and take possession of the Premises and expel or remove Tenant and any other person who may be occupying the Premises or any part thereof, without being liable for prosecution or any claim for damages therefor; and Landlord may recover from Tenant the following:

(i) The worth at the time of award of any unpaid rent which has been earned at the time of such termination; plus

(ii) The worth at the time of award of the amount by which the unpaid rent which would have been earned after termination until the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus

(iii) The worth at the time of award of the amount by which the unpaid rent for the balance of the Lease Term after the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus

(iv) Any other amount necessary to compensate Landlord for all the detriment proximately caused by Tenant's failure to perform its obligations under this Lease or which in the ordinary course of things would be likely to result therefrom, specifically including, but not limited to, brokerage commissions and advertising expenses incurred, expenses of remodeling the Premises or any portion thereof for a new tenant, whether for the same or a different use, and any special concessions made to obtain a new tenant; and

(v) At Landlord's election, such other amounts in addition to or in lieu of the foregoing as may be permitted from time to time by applicable law.

The term "rent" as used in this Section 18 shall be deemed to be and to mean all sums of every nature required to be paid by Tenant pursuant to the terms of this Lease, whether to Landlord or to others. As used in Sections 18(a)(i) and (ii) above, the "worth at the time of award" shall be computed by allowing interest at the Default Rate, but in no case greater than the maximum amount of such interest permitted by law. As used in Section 18(a)(iii) above, the "worth at the time of award" shall be computed by discounting such amount at the discount rate of the Federal Reserve Bank of San Francisco at the time of award plus one percent (1%).

(b) Landlord shall have the remedy described in California Civil Code Section 1951.4 (lessor may continue lease in effect after lessee's breach and abandonment and recover Rent as it becomes due, if lessee has the right to sublet or assign, subject only to reasonable limitations). Accordingly, if Landlord does not elect to terminate this Lease on account of any default by Tenant, Landlord may, from time to time, without terminating this Lease, enforce all of its rights and remedies under this Lease, including the right to recover all rent as it becomes due.

(c) **Subleases of Tenant.** Whether or not Landlord elects to terminate this Lease on account of any Event of Default by Tenant, as set forth in this Section 18, Landlord shall have the right to terminate any and all subleases, licenses, concessions or other consensual arrangements for possession entered into by Tenant and affecting the Premises or may, in Landlord's sole discretion, succeed to Tenant's interest in such subleases, licenses, concessions or arrangements. In the event of Landlord's election to succeed to Tenant's interest in any such subleases, licenses, concessions or arrangements, Tenant shall, as of the date of notice by Landlord of such election, have no further right to or interest in the rent or other consideration receivable thereunder.

(d) **Form of Payment After Default.** Following the occurrence of an Event of Default by Tenant, Landlord shall have the right to require that any or all subsequent amounts paid by Tenant to Landlord hereunder, whether in the cure of the default in question or otherwise, be paid in the form of cash, money order, cashier's or certified check drawn on an institution reasonably acceptable to Landlord, or by other means approved by Landlord, notwithstanding any prior practice of accepting payments in any different form.

(e) **Efforts to Relet.** For the purposes of this Section 18, Tenant's right to possession shall not be deemed to have been terminated by efforts of Landlord to relet the Premises, by its acts of maintenance or preservation with respect to the Premises, or by appointment of a receiver to protect Landlord's interests hereunder. The foregoing enumeration is not exhaustive, but merely illustrative of acts which may be performed by Landlord without terminating Tenant's right to possession.

(f) **Landlord Defaults and Tenant Remedies.** Except as otherwise provided in this Lease and specifically subject to Section 26(b), if Landlord fails in the performance of any of Landlord's obligations under this Lease and such failure continues for thirty (30) days after Landlord's receipt of written notice thereof from Tenant (and an additional reasonable time after such receipt if (A) such failure cannot be cured within such thirty (30) day period, and (B) Landlord commences curing such failure within such thirty (30) day period and thereafter diligently pursues the curing of such failure), then Tenant shall be entitled to exercise any remedies that Tenant may have at law or in equity. **TENANT WAIVES ANY RIGHT TO OBTAIN ANY CONSEQUENTIAL, SPECIAL, PUNITIVE, EXEMPLARY OR SIMILAR DAMAGES.**

#### 19. **Payment by Tenant; Non-Waiver; Cumulative Remedies.**

(a) **Payment by Tenant.** Upon any Event of Default, Tenant shall pay to Landlord all reasonable costs incurred by Landlord (including court costs and reasonable attorneys' fees and expenses) in: (1) obtaining possession of the Premises; (2) removing and storing Tenant's or any other occupant's property; (3) repairing, restoring, altering, remodeling, or otherwise putting the Premises into condition reasonably acceptable to a new tenant (provided that Tenant shall not be responsible for costs to change the character of the Premises from an office use to a primarily retail, industrial or other non-office type of use); (4) if Tenant is dispossessed of the Premises and this Lease is not terminated, reletting all or any part of the Premises (including brokerage commissions, cost of tenant finish work, and other costs incidental to such reletting); (5) performing Tenant's obligations which Tenant failed to perform; and (6) enforcing, or advising Landlord of, its rights, remedies, and recourses arising out of the Event of Default. To the full extent permitted by Law, Landlord and Tenant agree the federal and state courts of the state in which the Premises are located shall have exclusive jurisdiction over any matter relating to or arising from this Lease and the parties' rights and obligations under this Lease.

(b) **No Waiver.** Landlord's acceptance of Rent following an Event of Default shall not waive Landlord's rights regarding such Event of Default. No waiver by Landlord of any violation or breach of any of the terms contained herein shall waive Landlord's rights regarding any future violation of such term. Landlord's acceptance of any partial payment of Rent shall not waive Landlord's rights with regard to the remaining portion of the Rent that is due, regardless of any endorsement or other statement on any instrument delivered in payment of Rent or any writing delivered in connection therewith; accordingly, Landlord's acceptance of a partial payment of Rent shall not constitute an accord and satisfaction of the full amount of the Rent that is due.

(c) **Cumulative Remedies.** Any and all remedies set forth in this Lease: (1) shall be in addition to any and all other remedies Landlord may have at law or in equity; (2) shall be cumulative; and (3) may be pursued successively or concurrently as Landlord may elect. The exercise of any remedy by Landlord shall not be deemed an election of remedies or preclude Landlord from exercising any other remedies in the future.

20. **Intentionally Omitted.**

21. **Surrender of Premises.** No act by Landlord shall be deemed an acceptance of a surrender of the Premises, and no agreement to accept a surrender of the Premises shall be valid unless it is in writing and signed by Landlord. At the expiration or termination of this Lease, Tenant shall deliver to Landlord the Premises with all improvements located therein in good repair and condition, free of Hazardous Materials placed on the Premises during the Term (unless caused by Landlord, its employees, agents or contractors), in broom-clean condition including cleaning of interior surface of all walls, flooring, ceiling and/ or roof deck due to Tenant's specific use (with such cleaning by commercial cleaning application as approved by Landlord), reasonable wear and tear (and condemnation and Casualty damage, as to which Section 14 and Section 15 shall control) excepted, and shall deliver to Landlord all keys to the Premises. Tenant may remove all unattached trade fixtures, furniture, and personal property placed in the Premises or elsewhere in the Building by Tenant (but Tenant may not remove any such item which was paid for, in whole or in part, by Landlord or any wiring or cabling unless Landlord requires such removal). Additionally, at Landlord's option, Tenant shall (not later than ten (10) days after the expiration or earlier termination of the Lease) remove such alterations, additions (including stairs and bank vaults), improvements, trade fixtures, personal property, equipment, wiring, conduits, cabling and furniture (including Tenant's Off-Premises Equipment) as Landlord may request; however, Tenant shall not be required to remove the initial Tenant Improvements, nor shall Tenant be required to remove any other improvement or addition to the Premises or the Project if Landlord has specifically agreed in writing that such other improvement or addition in question need not be removed. Tenant shall repair all damage caused by such removal. All items not so removed shall, at Landlord's option, be deemed to have been abandoned by Tenant and may be appropriated, sold, stored, destroyed, or otherwise disposed of by Landlord at Tenant's cost without notice to Tenant and without any obligation to account for such items; any such disposition shall not be considered a strict foreclosure or other exercise of Landlord's rights in respect of the security interest granted under Section 20. The provisions of this Section 21 shall survive the expiration or earlier termination of the Lease.

22. **Holding Over.** If Tenant fails to vacate the Premises at the end of the Term, then Tenant shall be a tenant at sufferance and, in addition to all other damages and remedies to which Landlord may be entitled for such holding over, Tenant shall pay, in addition to the other Rent, (a) for the first two (2) months of such holdover period, Base Rent equal to one hundred twenty-five percent (125%) of the Base Rent payable during the last month of the Term, and (b) thereafter, Base Rent equal to one hundred fifty percent (150%) of the Base Rent payable during the last month of the Term (as applicable, the "**Holdover Rate**"), and Tenant shall otherwise continue to be subject to all of Tenant's obligations under this Lease. The provisions of this **Section 22** shall not be deemed to limit or constitute a waiver of any other rights or remedies of Landlord provided herein or at Law. **IF TENANT FAILS TO SURRENDER THE PREMISES UPON THE TERMINATION OR EXPIRATION OF THIS LEASE (EXCEPT AS SET FORTH IN THE FOLLOWING SENTENCE), IN ADDITION TO ANY OTHER LIABILITIES TO LANDLORD ACCRUING THEREFROM, TENANT SHALL PROTECT, DEFEND, INDEMNIFY AND HOLD LANDLORD HARMLESS FROM ALL LOSS, COSTS (INCLUDING REASONABLE ATTORNEYS' FEES) AND LIABILITY RESULTING FROM SUCH FAILURE, INCLUDING ANY CLAIMS MADE BY ANY SUCCEEDING TENANT FOUNDED UPON SUCH FAILURE TO SURRENDER, AND ANY LOST PROFITS TO LANDLORD RESULTING THEREFROM.** Notwithstanding the foregoing, if Tenant remains in the Premises at the end of the Term with the written consent of Landlord, then Tenant shall be a month-to-month tenant at the Holdover Rate, and Tenant shall otherwise continue to be subject to all of Tenant's obligations under this Lease.

23. **Certain Rights Reserved by Landlord.** Provided that the exercise of such rights does not unreasonably interfere with Tenant's occupancy of the Premises, Landlord shall have the following rights:

(a) **Building Operations.** To make inspections, repairs, alterations, additions, changes, or improvements, whether structural or otherwise, in and about the Project or Complex, as applicable, or any part thereof; to enter upon the Premises (after giving Tenant reasonable notice thereof, which may be oral notice, except in cases of real or apparent emergency, in which case no notice shall be required) and, during the continuance of any such work, to interrupt or temporarily suspend Building services and facilities; and to change the name of the Building;

(b) **Security.** To take such reasonable security measures as Landlord deems advisable (provided, however, that any such security measures are for Landlord's own protection, and Tenant acknowledges that Landlord is not a guarantor of the security or safety of any Tenant Party and that such security matters are the responsibility of Tenant); including evacuating the Building for cause, suspected cause, or for drill purposes; temporarily denying access to the Building;

(c) **Prospective Purchasers and Lenders.** To enter the Premises at all reasonable hours to show the Premises to prospective purchasers or lenders; and

(d) **Prospective Tenants.** At any time during the last twelve (12) months of the Term (or earlier if Tenant has notified Landlord in writing that it does not desire to renew the Term) or at any time following the occurrence of an Event of Default, to enter the Premises at all reasonable hours to show the Premises to prospective tenants.

24. [Intentionally Deleted].

25. Hazardous Materials.

(a) During the term of this Lease, Tenant shall comply with all Environmental Laws and Environmental Permits (each as defined in Section 25(i) below) applicable to the operation or use of the Premises, will cause all other persons occupying or using the Premises to comply with all such Environmental Laws and Environmental Permits, will immediately pay or cause to be paid all costs and expenses incurred by reason of such compliance, and will obtain and renew all Environmental Permits required for operation or use of the Premises.

(b) Tenant shall not generate, use, treat, store, handle, release or dispose of, or permit the generation, use, treatment, storage, handling, release or disposal of Hazardous Materials (as defined in Section 25(i) hereof) on the Premises, or the Complex, or transport or permit the transportation of Hazardous Materials to or from the Premises or the Complex except (i) for limited quantities used or stored at the Premises and required in connection with the routine operation and maintenance of the Premises such as office products and cleaning supplies, and then only in compliance with all applicable Environmental Laws, and (ii) as disclosed by Tenant in the Environmental Questionnaire attached as Exhibit I.

(c) At any time and from time to time during the term of this Lease, Landlord may perform an environmental site assessment report concerning the Premises, prepared by an environmental consulting firm chosen by Landlord, indicating the presence or absence of Hazardous Materials caused or permitted by Tenant and the potential cost of any compliance, removal or remedial action in connection with any such Hazardous Materials on the Premises. Tenant shall grant and hereby grants to Landlord and its agents access to the Premises and specifically grants Landlord an irrevocable non-exclusive license to undertake such an assessment. If such assessment report indicates the presence of Hazardous Materials caused or permitted by Tenant in violation of the terms of the Lease, then such report shall be at Tenant's sole cost and expense, and the cost of such assessment shall be immediately due and payable by Tenant to Landlord within thirty (30) days of receipt of an invoice therefor.

(d) Tenant will promptly advise Landlord in writing of any of the following: (1) any pending or threatened Environmental Claim (as defined in Section 25(i) below) against Tenant relating to the Premises or the Complex; (2) any condition or occurrence on the Premises or the Complex that (a) results in noncompliance by Tenant with any applicable Environmental Law, or (b) could reasonably be anticipated to form the basis of an Environmental Claim against Tenant or Landlord or the Premises; (3) any condition or occurrence on the Premises or any property adjoining the Premises that could reasonably be anticipated to cause the Premises to be subject to any restrictions on the ownership, occupancy, use or transferability of the Premises under any Environmental Law; and (4) the actual or anticipated taking of any removal or remedial action by Tenant in response to the actual or alleged presence of any Hazardous Material on the Premises or the Complex. All such notices shall describe in reasonable detail the nature of the claim, investigation, condition, occurrence or removal or remedial action and Tenant's response thereto. In addition, Tenant will provide Landlord with copies of all communications regarding the Premises with any governmental agency relating to Environmental Laws, all such communications with any person relating to Environmental Claims, and such detailed reports of any such Environmental Claim as may reasonably be requested by Landlord.

(e) Tenant will not change or permit to be changed the present use of the Premises unless Tenant shall have notified Landlord thereof in writing and Landlord shall have determined, in its sole and absolute discretion, that such change will not result in the presence of Hazardous Materials on the Premises except for those described in Section 25(b) above.

**(f) TENANT AGREES TO INDEMNIFY, DEFEND AND HOLD HARMLESS THE INDEMNITEES FROM AND AGAINST ALL OBLIGATIONS (INCLUDING REMOVAL AND REMEDIAL ACTIONS), LOSSES, CLAIMS, SUITS, JUDGMENTS, LIABILITIES, PENALTIES, DAMAGES (INCLUDING CONSEQUENTIAL AND PUNITIVE DAMAGES), COSTS AND EXPENSES (INCLUDING REASONABLE ATTORNEYS' AND CONSULTANTS' FEES AND EXPENSES) OF ANY KIND OR NATURE WHATSOEVER THAT MAY AT ANY TIME BE INCURRED BY, IMPOSED ON OR ASSERTED AGAINST SUCH INDEMNITEES DIRECTLY OR INDIRECTLY BASED ON, OR ARISING OR RESULTING FROM (A) THE ACTUAL OR ALLEGED PRESENCE OF HAZARDOUS MATERIALS ON THE COMPLEX WHICH IS CAUSED OR PERMITTED BY TENANT OR A TENANT PARTY AND (B) ANY ENVIRONMENTAL CLAIM RELATING IN ANY WAY TO TENANT'S OPERATION OR USE OF THE PREMISES (THE "TENANT HAZARDOUS MATERIALS INDEMNIFIED MATTERS"). THE FOREGOING INDEMNITY SHALL NOT INCLUDE ANY HAZARDOUS MATERIALS THAT WERE LOCATED AT THE PREMISES OR THE PROJECT ON THE DELIVERY DATE, NOR ANY HAZARDOUS MATERIALS PLACED ON THE PREMISES OR PROJECT BY LANDLORD, ITS EMPLOYEES, AGENTS, OR CONTRACTORS. THE PROVISIONS OF THIS SECTION 25 SHALL SURVIVE THE EXPIRATION OR SOONER TERMINATION OF THIS LEASE.**

**LANDLORD AGREES TO INDEMNIFY, DEFEND AND HOLD HARMLESS THE INDEMNITEES FROM AND AGAINST ALL OBLIGATIONS (INCLUDING REMOVAL AND REMEDIAL ACTIONS), LOSSES, CLAIMS, SUITS, JUDGMENTS, LIABILITIES, PENALTIES, DAMAGES (INCLUDING CONSEQUENTIAL AND PUNITIVE DAMAGES), COSTS AND EXPENSES (INCLUDING REASONABLE ATTORNEYS' AND CONSULTANTS' FEES AND EXPENSES) OF ANY KIND OR NATURE WHATSOEVER THAT MAY AT ANY TIME BE INCURRED BY, IMPOSED ON OR ASSERTED AGAINST SUCH INDEMNITEES DIRECTLY OR INDIRECTLY BASED ON, OR ARISING OR RESULTING FROM THE ACTUAL OR ALLEGED PRESENCE OF HAZARDOUS MATERIALS ON THE COMPLEX WHICH IS CAUSED OR PERMITTED BY LANDLORD OR A LANDLORD PARTY.**

(g) To the extent that the undertaking in the preceding paragraphs may be unenforceable because it is violative of any law or public policy, Tenant will contribute the maximum portion that it is permitted to pay and satisfy under applicable Law to the payment and satisfaction of all Tenant Hazardous Materials Indemnified Matters incurred by the Indemnitees.

(h) All sums paid and costs incurred by Landlord with respect to any Hazardous Materials Indemnified Matter shall bear interest at the Default Rate from the date so paid or incurred until reimbursed by Tenant, and all such sums and costs shall be immediately due and payable on demand.

(i) **"Hazardous Materials"** means (i) petroleum or petroleum products, natural or synthetic gas, asbestos in any form that is or could become friable, urea formaldehyde foam insulation, and radon gas; (ii) any substances defined as or included in the definition of "hazardous substances," "hazardous wastes," "hazardous materials," "extremely hazardous wastes," "restricted hazardous wastes," "toxic substances," "toxic pollutants," "contaminants" or "pollutants," or words of similar import, under any applicable Environmental Law; and (iii) any other substance exposure which is regulated by any governmental authority; (b) **"Environmental Law"** means any federal, state or local statute, law, rule, regulation, ordinance, code, policy or rule of common law now or hereafter in effect and in each case as amended, and any judicial or administrative interpretation thereof, including any judicial or administrative order, consent decree or judgment, relating to the environment, health, safety or Hazardous Materials, including without limitation, the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, 42 U.S.C. §§ 9601 et seq.; the Resource Conservation and Recovery Act, 42 U.S.C. §§ 6901 et seq.; the Hazardous Materials Transportation Act, 49 U.S.C. §§ 1801 et seq.; the Clean Water Act, 33 U.S.C. §§ 1251 et seq.; the Toxic Substances Control Act, 15 U.S.C. §§ 2601 et seq.; the Clean Air Act, 42 U.S.C. §§ 7401 et seq.; the Safe Drinking Water Act, 42 U.S.C. §§ 300f et seq.; the Atomic Energy Act, 42 U.S.C. §§ 2011 et seq.; the Federal Insecticide, Fungicide and Rodenticide Act, 7 U.S.C. §§ 136 et seq.; the Occupational Safety and Health Act, 29 U.S.C. §§ 651 et seq.; (c) **"Environmental Claims"** means any and all administrative, regulatory or judicial actions, suits, demands, demand letters, claims, liens, notices of non-compliance or violation, investigations, proceedings, consent orders or consent agreements relating in any way to any Environmental Law or any Environmental Permit, including without limitation (i) any and all Environmental Claims by governmental or regulatory authorities for enforcement, cleanup, removal, response, remedial or other actions or damages pursuant to any applicable Environmental Law and (ii) any and all Environmental Claims by any third party seeking damages, contribution, indemnification, cost recovery, compensation or injunctive relief resulting from Hazardous Materials or arising from alleged injury or threat of injury to health, safety or the environment; (d) **"Environmental Permits"** means all permits, approvals, identification numbers, licenses and other authorizations required under any applicable Environmental Law.

## 26. Miscellaneous.

(a) **Landlord Transfer.** Landlord may transfer any portion of the Building and any of its rights under this Lease. If Landlord assigns its rights under this Lease, then Landlord shall thereby be released from any further obligations hereunder arising after the date of transfer, provided that the assignee assumes Landlord's obligations hereunder in writing.

(b) **Landlord's Liability.** The liability of Landlord (and its partners, shareholders or members) to Tenant (or any person or entity claiming by, through or under Tenant) for any default by Landlord under the terms of this Lease or any matter relating to or arising out of the occupancy or use of the Premises and/or other areas of the Building or Complex shall be limited to Tenant's actual direct, but not consequential, damages therefor and shall be recoverable only from the interest of Landlord in the Building, and Landlord (and its partners, shareholders or members) shall not be personally liable for any deficiency. Landlord's liability to Tenant shall be further limited to Landlord's equity interest in the Project. **ADDITIONALLY, TO THE EXTENT ALLOWED BY LAW, TENANT HEREBY WAIVES ANY STATUTORY LIEN IT MAY HAVE AGAINST LANDLORD OR ITS ASSETS, INCLUDING WITHOUT LIMITATION, THE BUILDING.**

(c) **Force Majeure.** Other than for Tenant's obligations under this Lease that can be performed by the payment of money (e.g., payment of Rent and maintenance of insurance), whenever a period of time is herein prescribed for action to be taken by either party hereto, such party shall not be liable or responsible for, and there shall be excluded from the computation of any such period of time, any delays due to strikes, riots, acts of God, shortages of labor or materials, war, terrorism, governmental laws, regulations, or restrictions, or any other causes of any kind whatsoever which are beyond the control of such party (each a **"Force Majeure Event"**);

provided that in each case, the party seeking the extension of time due to the Force Majeure Event shall have notified the other party of the event or condition giving rise to any such delay within five (5) business days after the requesting party learns of the occurrence of the event or condition and thereafter regularly (but in no event less often than weekly) kept the other party apprised of the status. If the party seeking the extension of time due to the Force Majeure Event fails to give notice of an event or condition that otherwise constitutes a Force Majeure Event within five (5) business days after it learns of such event or condition or fails to keep the other party regularly apprised of the status of such event or condition, as applicable, then such event or condition shall not constitute a Force Majeure Event hereunder unless and until the requesting party gives a notice that such Force Majeure Event is continuing and specifying the date of onset of the Force Majeure Event, in which event the duration of such Force Majeure Event shall be limited to the period of continuation commencing on the date of such notice of continuation and shall be subject to the continuing obligation that the requesting party thereafter regularly (but no less often than weekly) keeps the other party apprised of the status.

(d) **Brokerage.** Neither Landlord nor Tenant has dealt with any broker or agent in connection with the negotiation or execution of this Lease, other than as set forth in the Basic Lease Information. **EACH PARTY SHALL INDEMNIFY, DEFEND AND HOLD HARMLESS THE OTHER PARTY FROM AND AGAINST ALL COSTS, EXPENSES, ATTORNEYS' FEES, LIENS AND OTHER LIABILITY FOR COMMISSIONS OR OTHER COMPENSATION CLAIMED BY ANY BROKER OR AGENT CLAIMING THE SAME BY, THROUGH, OR UNDER THE INDEMNIFYING PARTY.** The foregoing indemnity shall survive the expiration or earlier termination of the Lease.

(e) **Estoppel Certificates.** From time to time, Tenant shall furnish to any party designated by Landlord, within ten (10) days after Landlord has made a request therefor, a certificate signed by Tenant confirming and containing such factual certifications and representations as to this Lease as Landlord may reasonably request. Unless otherwise required by Landlord's Mortgagee or a prospective purchaser or mortgagee of the Building, the initial form of estoppel certificate to be signed by Tenant is attached hereto as Exhibit G.

(f) **Notices.** All notices and other communications given pursuant to this Lease shall be in writing and shall be: (1) mailed by first class, United States Mail, postage prepaid, certified, with return receipt requested, and addressed to the parties hereto at the address specified in the Basic Lease Information; (2) hand delivered to the intended addressee; (3) sent by a nationally recognized overnight courier service; or (4) sent by facsimile transmission during normal business hours followed by a copy of such notice sent in another manner permitted hereunder. All notices shall be effective upon the earlier to occur of actual receipt, one (1) Business Day following deposit with a nationally recognized overnight courier service, or three (3) days following deposit in the United States mail. The parties hereto may change their addresses by giving notice thereof to the other in conformity with this provision.

(g) **Separability.** If any clause or provision of this Lease is illegal, invalid, or unenforceable under present or future laws, then the remainder of this Lease shall not be affected thereby and in lieu of such clause or provision, there shall be added as a part of this Lease a clause or provision as similar in terms to such illegal, invalid, or unenforceable clause or provision as may be possible and be legal, valid, and enforceable.

(h) **Amendments; Binding Effect.** This Lease may not be amended except by instrument in writing signed by Landlord and Tenant. No provision of this Lease shall be deemed to have been waived by Landlord unless such waiver is in writing signed by Landlord, and no custom or practice which may evolve between the parties in the administration of the terms hereof shall waive or diminish the right of Landlord to insist upon the performance by Tenant in strict accordance with the terms hereof. The terms and conditions contained in this Lease shall inure to the benefit of and be binding upon the parties hereto, and upon their respective successors in interest and legal representatives, except as otherwise herein expressly provided. This Lease is for the sole benefit of Landlord and Tenant, and, other than Landlord's Mortgagee, no third party shall be deemed a third party beneficiary hereof.

(i) **Quiet Enjoyment.** Provided Tenant has performed all of its obligations hereunder, Tenant shall peaceably and quietly hold and enjoy the Premises for the Term, without hindrance from Landlord or any party claiming by, through, or under Landlord, but not otherwise, subject to the terms and conditions of this Lease.

(j) **No Merger.** There shall be no merger of the leasehold estate hereby created with the fee estate in the Premises or any part thereof if the same person acquires or holds, directly or indirectly, this Lease or any interest in this Lease and the fee estate in the leasehold Premises or any interest in such fee estate.

(k) **No Offer.** The submission of this Lease to Tenant shall not be construed as an offer, and Tenant shall not have any rights under this Lease unless Landlord executes a copy of this Lease and delivers it to Tenant.

(l) **Entire Agreement.** This Lease constitutes the entire agreement between Landlord and Tenant regarding the subject matter hereof and supersedes all oral statements and prior writings relating thereto. Except for those set forth in this Lease, no representations, warranties, or agreements have been made by Landlord or Tenant to the other with respect to this Lease or the

obligations of Landlord or Tenant in connection therewith. The normal rule of construction that any ambiguities be resolved against the drafting party shall not apply to the interpretation of this Lease or any exhibits or amendments hereto.

(m) **Waiver of Jury Trial.** TO THE MAXIMUM EXTENT PERMITTED BY LAW, LANDLORD AND TENANT EACH WAIVE ANY RIGHT TO TRIAL BY JURY IN ANY LITIGATION OR TO HAVE A JURY PARTICIPATE IN RESOLVING ANY DISPUTE ARISING OUT OF OR WITH RESPECT TO THIS LEASE OR ANY OTHER INSTRUMENT, DOCUMENT OR AGREEMENT EXECUTED OR DELIVERED IN CONNECTION HEREWITH OR THE TRANSACTIONS RELATED HERETO.

(n) **Governing Law.** This Lease shall be governed by and construed in accordance with the laws of the state in which the Premises are located.

(o) **Recording.** Tenant shall not record this Lease or any memorandum of this Lease without the prior written consent of Landlord, which consent may be withheld or denied in the sole and absolute discretion of Landlord, and any recordation by Tenant shall be a material breach of this Lease. Tenant grants to Landlord a power of attorney to execute and record a release releasing any such recorded instrument of record that was recorded without the prior written consent of Landlord, which power of attorney is coupled with an interest and is non-revocable during the Term.

(p) **Joint and Several Liability.** If Tenant is comprised of more than one (1) party, each such party shall be jointly and severally liable for Tenant's obligations under this Lease. All unperformed obligations of Tenant hereunder not fully performed at the end of the Term shall survive the end of the Term, including payment obligations with respect to Rent and all obligations concerning the condition and repair of the Premises.

(q) **Financial Reports.** Within thirty (30) days after Landlord's request, Tenant will furnish Tenant's most recent audited financial statements (including any notes to them) to Landlord, or, if no such audited statements have been prepared, such other financial statements (and notes to them) as may have been prepared by an independent certified public accountant or, failing those, Tenant's internally prepared financial statements. If Tenant is a publicly traded corporation, Tenant may satisfy its obligations hereunder by providing to Landlord Tenant's most recent annual and quarterly reports. Landlord will not disclose any aspect of Tenant's financial statements that Tenant designates to Landlord as confidential except: (1) to Landlord's Mortgagee or prospective mortgagees or purchasers of the Building; (2) in litigation between Landlord and Tenant; and (3) if required by court order. Tenant shall not be required to deliver the financial statements required under this Section 26(q) more than once in any twelve (12) month period unless requested by Landlord's Mortgagee or a prospective buyer or lender of the Building or an Event of Default occurs.

(r) **Landlord's Fees.** Whenever Tenant requests Landlord to take any action not required of it hereunder or give any consent required or permitted under this Lease, Tenant will reimburse Landlord for Landlord's reasonable, out-of-pocket costs payable to third parties and incurred by Landlord in reviewing the proposed action or consent, including reasonable attorneys', engineers' or architects' fees, within thirty (30) days after Landlord's delivery to Tenant of a statement of such costs. Tenant will be obligated to make such reimbursement without regard to whether Landlord consents to any such proposed action.

(s) **Telecommunications.** Except as provided hereinbelow, Tenant and its telecommunications companies, including local exchange telecommunications companies and alternative access vendor services companies, shall have no right of access to and within the Building, for the installation and operation of telecommunications systems, including voice, video, data, Internet, and any other services provided over wire, fiber optic, microwave, wireless, and any other transmission systems ("**Telecommunications Services**"), for part or all of Tenant's telecommunications within the Building and from the Building to any other location without Landlord's prior written consent. All providers of Telecommunications Services shall be required to comply with the rules and regulations of the Building, applicable Laws and Landlord's policies and practices for the Building. Tenant acknowledges that Landlord shall not be required to provide or arrange for any Telecommunications Services and that Landlord shall have no liability to any Tenant Party in connection with the installation, operation or maintenance of Telecommunications Services or any equipment or facilities relating thereto. Tenant, at its cost and for its own account, shall be solely responsible for obtaining all Telecommunications Services.

Notwithstanding the foregoing to the contrary, if Tenant requires the installation of one or more satellite dishes or other data transmission equipment on the roof of the Building (collectively, the "**Telecommunications Equipment**"), then upon thirty (30) days advance written notice to Landlord and subject to available capacity and Tenant's compliance with all applicable laws and Landlord's requirements for property and roof maintenance and repair, Tenant may place such Telecommunications Equipment on the roof of the Premises in a location reasonably approved by Landlord. The installation of the Telecommunications Equipment shall constitute an Alteration and shall be performed in accordance with and subject to the provisions of Article 8 of this Lease, and the Telecommunications Equipment shall be treated for all purposes of the Lease as if the same were Tenant's property. The cost of the Telecommunications Equipment and all costs of installing, maintaining and removing the Telecommunications Equipment shall be borne solely by Tenant. Upon the expiration of the Term or upon any earlier termination of the Lease, Tenant shall, at Tenant's sole

cost and expense and subject to the control of and direction from Landlord, remove the Telecommunications Equipment, repair and damage caused thereby, and restore the roof to the condition existing prior to the installation of the Telecommunications Equipment, reasonable wear and tear excepted.

(t) **Authority.** Tenant (if a corporation, partnership or other business entity) hereby represents and warrants to Landlord that Tenant is a duly formed and existing entity qualified to do business in the state in which the Premises are located, that Tenant has full right and authority to execute and deliver this Lease, and that each person signing on behalf of Tenant is authorized to do so.

(u) **Waiver.** LANDLORD AND TENANT EXPRESSLY DISCLAIM ANY IMPLIED WARRANTY THAT THE PREMISES ARE SUITABLE FOR TENANT'S INTENDED COMMERCIAL PURPOSE, AND TENANT'S OBLIGATION TO PAY RENT HEREUNDER IS NOT DEPENDENT UPON THE CONDITION OF THE PREMISES OR THE PERFORMANCE BY LANDLORD OF ITS OBLIGATIONS HEREUNDER, AND, EXCEPT AS OTHERWISE EXPRESSLY PROVIDED HEREIN, TENANT SHALL CONTINUE TO PAY THE RENT, WITHOUT ABATEMENT, DEMAND, SETOFF OR DEDUCTION, NOTWITHSTANDING ANY BREACH BY LANDLORD OF ITS DUTIES OR OBLIGATIONS HEREUNDER, WHETHER EXPRESS OR IMPLIED. TO THE EXTENT ALLOWED BY LAW, TENANT WAIVES THE BENEFIT OF ANY CONSUMER PROTECTION LAWS.

(v) **Tenant Representation.** Tenant is not a person or entity described by Sec. 1 of the Executive Order (No. 13,224) Blocking Property and Prohibiting Transactions With Persons Who Commit, Threaten to Commit, or Support Terrorism, 66 Fed. Reg. 49,079 (Sept. 24, 2001), and does not engage in any dealings or transactions, and is not otherwise associated, with any such persons or entities.

(w) **Transportation Management.** Tenant shall comply with all present or future programs having the force of law intended to manage parking, transportation or traffic in and around the Complex, and in connection therewith, Tenant shall take responsible action for the transportation planning and management of all employees located at the Premises by working directly with Landlord, any governmental transportation management organization or any other transportation-related committees or entities.

(x) **CC&Rs; Disclosure.** Tenant acknowledges that this Lease is subject to (i) that certain Declaration of Covenants, Conditions and Restrictions for Koll Center Sierra Point, dated October 9, 1984, and recorded on October 17, 1984 as Instrument No. 84112690 in the Official Records of San Mateo County, California (as the same has been and may be amended), and (ii) that certain Declaration of Covenants, Conditions and Environmental Restrictions Relating to Environmental Compliance for Sierra Point, dated October 21, 1998 and recorded on October 23, 1998 as Instrument No. 98-172219 in the Official Records of San Mateo County, California (as the same has been and may be amended) (collectively, the "CC&Rs"). Tenant acknowledges that (i) the Complex consists of property formerly used as a municipal landfill, (ii) methane barriers have been installed beneath the Premises, and (iii) methane levels are monitored throughout the Complex in accordance with the terms of the CC&Rs. The taking of possession of the Premises by Tenant shall be conclusive evidence that Tenant accepts the same "AS-IS" and that the Premises is suited for the use intended by Tenant and is in good and satisfactory condition at the time such possession was taken.

(y) **Disclosure.** Tenant hereby waives any and all rights under and benefits of California Civil Code Section 1938 and acknowledges that neither the Complex, the Project nor the Premises has undergone inspection by a Certified Access Specialist (CASp) (defined in California Civil Code Section 55.52).

**[SIGNATURES ON FOLLOWING PAGE]**

This Lease is executed on the respective dates set forth below, but for reference purposes, this Lease shall be dated as of the date first above written. If the execution date is left blank, this Lease shall be deemed executed as of the date first written above.

**LANDLORD:**

MARINA BOULEVARD PROPERTY, LLC,  
a Delaware limited liability company

By: /s/ W.Greg Geiger  
Printed Name: W.Greg Geiger  
Title: Authorized Signer

By: /s/ Sean Armstrong  
Printed Name: Sean Armstrong  
Title: Authorized Signer

Execution Date: December 8, 2015

**TENANT:**

ULTRAGENYX PHARMACEUTICAL INC.,  
a Delaware corporation

By: /s/ Tom Kassberg  
Printed Name: Tom Kassberg  
Title: CBO

By: \_\_\_\_\_  
Printed Name: \_\_\_\_\_  
Title: \_\_\_\_\_

Execution Date: December 8, 2015

EXHIBIT A-1

SITE PLAN DEPICTING PREMISES AND BUILDING

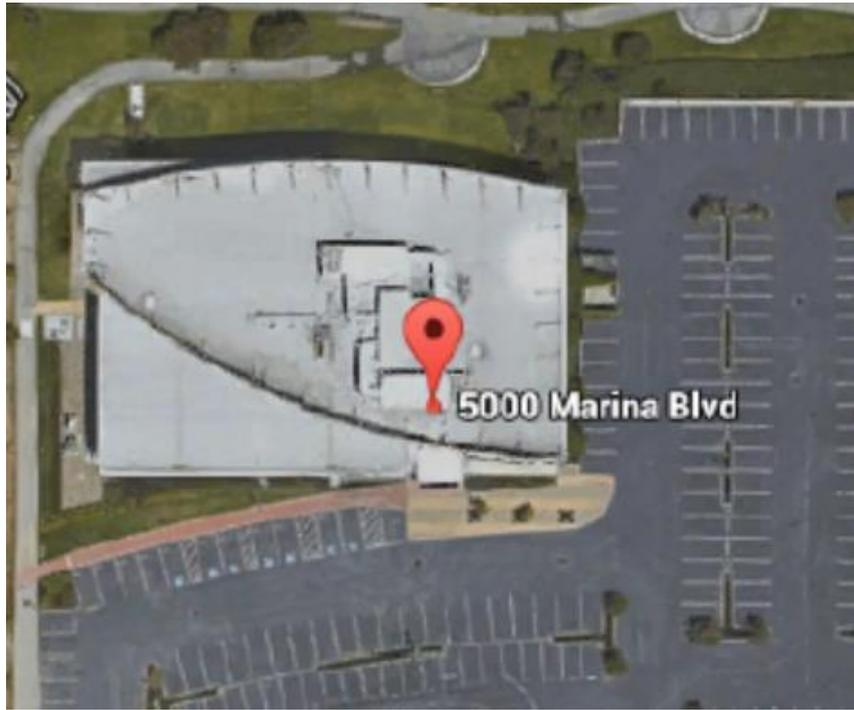


EXHIBIT A-1

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EXHIBIT A-2

SITE PLAN DEPICTING COMPLEX

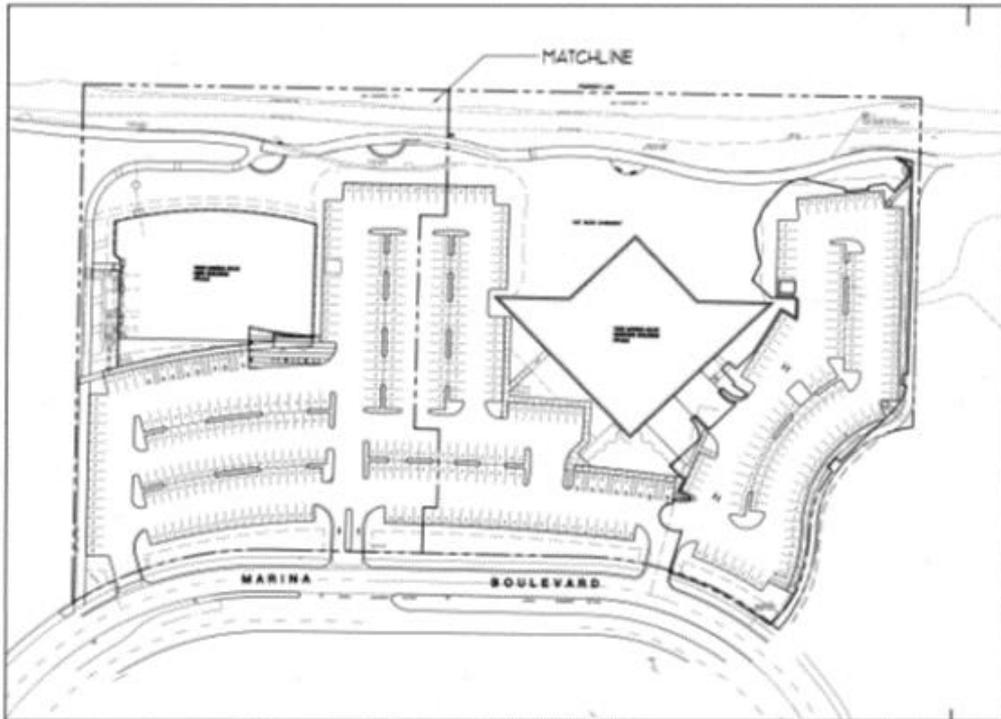


EXHIBIT A-2

**EXHIBIT B**

**LEGAL DESCRIPTION OF THE LAND**

THE LAND REFERRED TO HEREIN BELOW IS SITUATED IN THE CITY OF BRISBANE, IN THE COUNTY OF SAN MATEO, STATE OF CALIFORNIA, AND IS DESCRIBED AS FOLLOWS:

**Parcel One:**

Parcel A as shown on that certain map entitled "Parcel Map, Lands of Foster Enterprises, a General Partnership" filed for record in the Office of the Recorder of the County of Sank Mateo, State of California on November 6, 2000 in Book 73 of Parcel Maps at page 27.

Excepting all minerals and all mineral rights of every kind and character now known to exist or hereafter discovered, including without limiting the generality of the foregoing, oil and gas and rights thereto, together with the sole, exclusive, and perpetual right to explore for, remove and dispose of said minerals by any means or methods suitable to the grantor, it's successors and assigns including lateral or slant drilling, but without entering upon to using the surface of the lands hereby conveyed, and in such manner as not to damage the surface of said lands or any building located thereon or hereafter erected thereon or the substructure of any such building, or to interfere with the use thereof by the grantee, it's successors or assigns, as excepted in the following Deeds to Utah Constructing & Mining Co., a Corporation, predecessor in interest to the vestees herein:

A. From Marie Louise Philips, dated August 20, 1959 and recorded September 14, 1959, Instrument no. 86272-R, in Book 3670 of Official Records at page 624.

B. From John F. Wilcox, dated August 27, 1959 and recorded September 14, 1959, Instrument no. 86273-R, in Book 3670 of Official Records at page 625.

C. From Marita Clark, dated August 20, 1959 and recorded September 14, 1959, Instrument no. 86274-R in Book 3670 of Official Records at page 626.

APN: 007-165-110

**Parcel Two:**

Parcel B as shown on that certain map entitled "Parcel Map, Lands of Foster Enterprises, a General Partnership" filed for record in the Office of the Recorder of the County of Sank Mateo, State of California on November 6, 2000 in Book 73 of Parcel Maps at page 27.

Excepting all minerals and all mineral rights of every kind and character now known to exist or hereafter discovered, including without limiting the generality of the foregoing, oil and gas and rights thereto, together with the sole, exclusive, and perpetual right to explore for, remove and dispose of said minerals by any means or methods suitable to the grantor, it's successors and assigns including lateral or slant drilling, but without entering upon or using the surface of the lands hereby conveyed, and in such manner as not to damage the surface of said lands or any building located thereon or hereafter erected thereon or the substructure of any such building, or to interfere with the use thereof by the grantee, it's successors or assigns, as excepted in the following Deeds to Utah Constructing & Mining Co., a Corporation, predecessor in interest to the vestees herein:

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C. From Marita Clark, dated August 20, 1959 and recorded September 14, 1959, Instrument no. 86274-R in Book 3670 of Official Records at page 626.

APN: 007-165-120

APN: 007-165-110, 007-165-120

**EXHIBIT B**

## EXHIBIT C

### ADDITIONAL RENT, TAXES, AND INSURANCE

1. **Additional Rent.** Tenant shall pay to Landlord all costs of Common Area Maintenance Costs, Taxes, and Insurance for the Building, and Tenant's Proportionate Share of the annual Common Area Maintenance Costs (defined below) in the Complex ("**Additional Rent**"). Landlord may make a good faith estimate of the Additional Rent to be due by Tenant for any calendar year or part thereof during the Term. During each calendar year or partial calendar year of the Term, Tenant shall pay to Landlord, in advance concurrently with each monthly installment of Base Rent, an amount equal to the estimated Additional Rent for such calendar year or part thereof divided by the number of months therein. From time to time, Landlord may estimate and re-estimate the Additional Rent to be due by Tenant and deliver a copy of the estimate or re-estimate to Tenant. Thereafter, the monthly installments of Additional Rent payable by Tenant shall be appropriately adjusted in accordance with the estimations so that, by the end of the calendar year in question, Tenant shall have paid all of the Additional Rent as estimated by Landlord. Any amounts paid based on such an estimate shall be subject to adjustment as herein provided when actual Common Area Maintenance Costs are available for each calendar year.

2. **Common Area Maintenance Costs.** The term "**Common Area Maintenance Costs**" shall mean all expenses and disbursements (subject to the limitations set forth below) that Landlord incurs in connection with the ownership, operation, and maintenance of the Project or Complex, as applicable, determined in accordance with sound accounting principles consistently applied, including the following costs: (a) wages and salaries of all on-site employees at or below the grade of senior building manager engaged in the operation, maintenance, repair or security of the Project or Complex, as applicable, including taxes, insurance and benefits relating thereto (together with Landlord's reasonable allocation of expenses of off-site employees at or below the grade of senior building manager who perform a portion of their services in connection with the operation, maintenance or security of the Project or Complex, as applicable; provided, that if any such employees of Landlord provide services for more than one building of Landlord, then a prorated portion of such employees' wages, benefits and taxes shall be included in Common Area Maintenance Costs based on the portion of their working time devoted to the Project or Complex, as applicable); (b) all supplies and materials used in the operation, maintenance, repair, replacement, and security of the Project or Complex, as applicable; (c) costs for improvements made to the Project or Complex, as applicable which, although capital in nature, are (i) expected to reduce the normal Common Area Maintenance Costs (including all utility costs) of the Project or Complex, as applicable, as amortized using a commercially reasonable interest rate over the time period reasonably estimated by Landlord to recover the costs thereof taking into consideration the anticipated cost savings, as determined by Landlord using its good faith, commercially reasonable judgment, as well as (ii) capital improvements made in order to comply with any Law hereafter promulgated by any governmental authority or any interpretation hereafter rendered with respect to any existing Law, as amortized using a commercially reasonable interest rate over the useful economic life of such improvements as determined by Landlord in its reasonable discretion, as well as (iii) capital improvements made to improve the health, safety and welfare of the Building and its occupants, as amortized using a commercially reasonable interest rate over the useful economic life of such improvements as determined by Landlord in its reasonable discretion; (d) cost of all utilities used in the Common Areas; (e) repairs, replacements, and general maintenance of the Project or Complex, including common area maintenance fees charged by an owner's association and reasonable market-rate property management fees charged by Owner's property manager or by Owner, as applicable; (f) fair market rental and other costs with respect to the management office for the Building or Complex, if any; (g) service, maintenance and management contracts with independent contractors for the operation, maintenance, management, repair, replacement, or security of the Project or Complex, as applicable, including the Common Areas; and (h) payments under any easement, license, operating agreement, declaration, restrictive covenant, or instrument now or hereafter affecting the Complex, including, without limitation, the Declaration of Covenants, Conditions and Restrictions for Koll Center Sierra Point, dated October 9, 1984, and recorded on October 17, 1984 as Instrument No. 84112690 in the Official Records of San Mateo County, California (as the same has been and may be amended), and the Declaration of Covenants, Conditions and Environmental Restrictions Relating to Environmental Compliance for Sierra Point, dated October 21, 1998 and recorded on October 23, 1998 as Instrument No. 98-172219 in the Official Records of San Mateo County, California (as the same has been and may be amended). If the Building is part of a Complex, Common Area Maintenance Costs may be prorated among the Project and the other buildings of the Complex, as reasonably determined by Landlord.

Common Area Maintenance Costs shall not include costs for: (1) repair, replacements and general maintenance paid by proceeds of insurance or by Tenant or other third parties; (2) interest, amortization or other payments on loans to Landlord; (3) depreciation; (4) leasing commissions; (5) legal expenses; (6) renovating or otherwise improving space for leased premises of the Project or Complex, as applicable or vacant space in the Project or Complex, as applicable; (7) Taxes and Insurance which are paid separately pursuant to Sections 3 and 4 below; (8) federal, state and local income taxes imposed on or measured by the income of Landlord from the operation of the Project or Complex, as applicable; (9) capital improvements made to the Project or Complex, as applicable, other than capital improvements described in Section 2 of this Exhibit and except for items which are generally considered maintenance and repair items, such as painting of Common Areas, and the like; (10) the cost of correcting defects in the construction of the Building or in the Building Systems; (11) salaries of officers and executives of Landlord; (12) the cost of any work or service

## EXHIBIT C

performed for any tenant of the Building (other than Tenant) to a materially greater extent or in a materially more favorable manner than that furnished generally to the tenants and other occupants (including Tenant); (13) all costs of cleanup, removal, investigation and/or remediation (collectively, "**Remediation Costs**") of any Hazardous Substances in, on or under the Project the extent such Hazardous Substances are (x) in existence as of the Delivery Date and in violation of applicable Laws, or (y) introduced onto the Project after the Delivery Date by Landlord or any of Landlord's agents, employees, contractors or tenants or other third parties not related to Tenant in violation of applicable Laws; (14) the cost of any repairs, alterations, additions, changes, replacements and other items which are made in order to prepare for a new tenant's occupancy; (15) any advertising expenses; (16) any costs included in Common Area Maintenance Costs representing an amount paid to a corporation related to Landlord which is in excess of the amount which would have been paid in the absence of such relationship; (17) interest and penalties due to late payment of any amounts owed by Landlord, except such as may be incurred as a result of Tenant's failure to timely pay its portion of such amounts or as a result of Landlord's contesting such amounts in good faith; (18) costs related to the existence and maintenance of Landlord as a legal entity, except to the extent attributable to the operation and management of the Project or Complex, as applicable; (19) the cost of any work or service performed for any tenant (including Tenant) at such tenant's cost; (20) political or charitable contributions; and (21) ground rent payable under any ground lease.

3. **Taxes.** Tenant shall pay all Taxes for the Building, and Tenant's Proportionate Share of Taxes for the Complex for each year and partial year falling within the Term. Tenant shall pay Tenant's Proportionate Share of Taxes in the same manner as provided above for Tenant's Proportionate Share of Common Area Maintenance Costs. "**Taxes**" shall mean taxes, assessments, and governmental charges or fees whether federal, state, county or municipal, and whether they be by taxing districts or authorities presently taxing or by others, subsequently created or otherwise, and any other taxes and assessments (including non-governmental assessments for common charges under a restrictive covenant or other private agreement that are not treated as part of Common Area Maintenance Costs) now or hereafter attributable to the Project or Complex, as applicable (or its operation), excluding, however, penalties and interest thereon and federal and state taxes on income (if the present method of taxation changes so that in lieu of or in addition to the whole or any part of any Taxes, there is levied on Landlord a capital tax directly on the rents received therefrom or a franchise tax, assessment, or charge based, in whole or in part, upon such rents for the Project or Complex, as applicable, then all such taxes, assessments, or charges, or the part thereof so based, shall be deemed to be included within the term "Taxes" for purposes hereof). Taxes shall include the costs of consultants retained in an effort to lower taxes and all costs incurred in disputing any taxes or in seeking to lower the tax valuation of the Project. Taxes shall also include any assessment, tax, fee, levy or charge in addition to, or in substitution, partially or totally, of any assessment, tax, fee, levy or charge previously included within the definition of real property tax, it being acknowledged by Tenant and Landlord that Proposition 13 was adopted by the voters of the State of California in the June 1978 election ("**Proposition 13**") and that assessments, taxes, fees, levies and charges may be imposed by governmental agencies for such services as fire protection, street, sidewalk and road maintenance, conservation, refuse removal and for other governmental services formerly provided without charge to property owners or occupants, and, in further recognition of the decrease in the level and quality of governmental services and amenities as a result of Proposition 13, Taxes shall also include any governmental or private assessments or the Building's or Complex's contribution towards a governmental or private cost-sharing agreement for the purpose of augmenting or improving the quality of services and amenities normally provided by governmental agencies. It is the intention of Tenant and Landlord that all such new and increased assessments, taxes, fees, levies, and charges and all similar assessments, taxes, fees, levies and charges be included within the definition of Taxes for purposes of this Lease. Tenant shall reimburse Landlord, as Additional Rent, upon demand for any and all taxes required to be paid by Landlord (except to the extent included in Taxes for the Complex by Landlord), excluding state, local and federal personal or corporate income taxes measured by the net income of Landlord from all sources and estate and inheritance taxes, whether or not now customary or within the contemplation of the parties hereto, when: (a) said taxes are measured by or reasonably attributable to the cost or value of Tenant's equipment, furniture, fixtures and other personal property located in the Premises, or by the cost or value of any leasehold improvements made in or to the Premises by or for Tenant, including the Tenant Improvements, to the extent the cost or value of such leasehold improvements exceeds the cost or value of a building standard build out as determined by Landlord regardless of whether title to such improvements shall be vested in Tenant or Landlord; (b) said taxes are assessed upon or with respect to the possession, leasing, operation, management, maintenance, alteration, repair, use or occupancy by Tenant of the Premises or any portion of the Complex used by Tenant in connection with this Lease; or (c) said taxes are assessed upon this transaction or any document to which Tenant is a party creating or transferring an interest or an estate in the Premises.

4. **Insurance.** Tenant shall pay all Insurance for the Building, and Tenant's Proportionate Share of Insurance for the Complex for each year and partial year falling within the Term. Tenant shall pay Tenant's Proportionate Share of Insurance in the same manner as provided above for Tenant's Proportionate Share of Common Area Maintenance Costs. "**Insurance**" shall mean property, liability and other insurance coverages carried by Landlord, including without limitation deductibles and risk retention programs and an allocation of a portion of the cost of blanket insurance policies maintained by Landlord and/or its affiliates.

5. **Common Area Maintenance, Tax and Insurance Statement.** By May 1 of each calendar year, or as soon thereafter as practicable, Landlord shall furnish to Tenant a statement of Common Area Maintenance Costs, Taxes, and Insurance for the Complex

EXHIBIT C

for the previous year, adjusted as provided in Section 6 of this Exhibit (the “**Common Area Maintenance, Tax and Insurance Statement**”). If Tenant’s estimated payments of Common Area Maintenance or Taxes or Insurance for the Complex under this Exhibit C for the year covered by the Common Area Maintenance Costs, Tax and Insurance Statement exceed Tenant’s share of such items as indicated in the Common Area Maintenance, Tax and Insurance Statement, then Landlord shall promptly credit or reimburse Tenant for such excess; likewise, if Tenant’s estimated payments of Common Area Maintenance, Taxes and Insurance under this Exhibit C for such year are less than Tenant’s share of such items as indicated in the Common Area Maintenance, Tax and Insurance Statement, then Tenant shall promptly pay Landlord such deficiency, notwithstanding that the Term has expired and Tenant has vacated the Premises.

Within one hundred eighty (180) days after receipt of a Common Area Maintenance, Tax and Insurance Statement by Tenant, if Tenant disputes the amount of Additional Rent set forth in the Common Area Maintenance, Tax and Insurance Statement, a reputable certified public accountant (which accountant has had previous experience in reviewing financial operating records of landlords of office buildings; provided that such accountant is not retained by Tenant on a contingency fee basis), designated and paid for by Tenant, may, after reasonable notice to Landlord and at reasonable times, inspect Landlord’s records at Landlord’s offices, provided that Tenant is not then in default under this Lease. In connection with such inspection, Tenant and Tenant’s agents must agree in advance to abide by Landlord’s reasonable rules and procedures regarding inspections of Landlord’s records, and shall execute a commercially reasonable confidentiality agreement regarding such inspection. Tenant’s failure to dispute the amount of Additional Rent set forth in any Common Area Maintenance, Tax and Insurance Statement within one hundred eighty (180) days of Tenant’s receipt of such Common Area Maintenance, Tax and Insurance Statement shall be deemed to be Tenant’s approval of such Common Area Maintenance, Tax and Insurance Statement and Tenant, thereafter, waives the right or ability to dispute the amounts set forth in such Common Area Maintenance, Tax and Insurance Statement. If after such inspection, Tenant still disputes such Additional Rent, a certification as to the proper amount shall be made, at Tenant’s expense, by an independent certified public accountant (the “**Accountant**”) selected by Landlord and subject to Tenant’s reasonable approval; provided that if such certification by the Accountant proves that Additional Rent were overstated by more than four percent (4%), then the cost of the Accountant and the cost of such certification shall be paid for by Landlord. In no event shall this Section 5 be deemed to allow any review of any Landlord’s records by any subtenant of Tenant (approved by Landlord). Tenant agrees that this Section 5 shall be the sole method to be used by Tenant to dispute the amount of any Additional Rent payable or not payable by Tenant pursuant to the terms of this Lease, and Tenant hereby waives any other rights at law or in equity relating thereto.

6. **Gross-Up.** With respect to any calendar year or partial calendar year in which the Complex is not occupied to the extent of 95% of the rentable area thereof, or Landlord is not supplying services to 95% of the rentable area thereof, the portion of Common Area Maintenance Costs for such period which vary by occupancy shall, for the purposes hereof, be increased to the amount which would have been incurred had the Complex been occupied to the extent of 95% of the rentable area thereof and Landlord had been supplying services to 95% of the rentable area thereof.

EXHIBIT C

**EXHIBIT D**

**TENANT WORK LETTER**

This Work Letter (“**Work Letter**”) sets forth the terms and conditions relating to the construction of improvements for the Premises. All references in this Work Letter to the “Lease” shall mean the relevant portions of the Lease to which this Work Letter is attached as Exhibit D.

**SECTION 1**

**BASE, SHELL AND CORE**

Except for the Allowance, the Additional Allowance and the FF&E Allowance (as such terms are defined below), Landlord shall not be obligated to make or pay for any alterations or improvements to the Premises, the Building or the Project. In addition to the construction of the Tenant Improvements, Landlord shall perform the Landlord Work described on Schedule D-1 attached hereto at Landlord’s sole expense and cost.

**SECTION 2**

**CONSTRUCTION DRAWINGS FOR THE PREMISES**

Promptly following execution of this Lease, Landlord and Tenant shall approve a detailed space plan for the construction of certain improvements in the Premises, which space plan shall be prepared by Design Blitz (the “**Final Space Plan**”). Based upon and in conformity with the Final Space Plan, Landlord shall cause its architect and engineers to prepare and deliver to Tenant, for Tenant’s approval, detailed specifications and engineered working drawings for the tenant improvements shown on the Final Space Plan (the “**Working Drawings**”). The Working Drawings shall incorporate modifications to the Final Space Plan as necessary to comply with the floor load and other structural and system requirements of the Building. To the extent that the finishes and specifications are not completely set forth in the Final Space Plan for any portion of the tenant improvements depicted thereon, the actual specifications and finish work shall be in accordance with the specifications for the Building’s standard tenant improvement items (“**Specifications**”), as determined by Landlord. Within five (5) business days after Tenant’s receipt of the Working Drawings, Tenant shall approve or disapprove the same, which approval shall not be unreasonably withheld; provided, however, that Tenant may only disapprove the Working Drawings to the extent such Working Drawings are inconsistent with the Final Space Plan and only if Tenant delivers to Landlord, within such five (5) business-day period, specific changes proposed by Tenant which are consistent with the Final Space Plan and do not constitute changes which would result in any of the circumstances described in items (i) through (iv) below. If any such revisions are timely and properly proposed by Tenant, Landlord shall cause its architect and engineers to revise the Working Drawings to incorporate such revisions and submit the same for Tenant’s approval in accordance with the foregoing provisions, and the parties shall follow the foregoing procedures for approving the Working Drawings until the same are finally approved by Landlord and Tenant. Upon Landlord’s and Tenant’s approval of the Working Drawings, the same shall be known as the “**Approved Working Drawings**”. The tenant improvements shown on the Approved Working Drawings shall be referred to herein as the “**Tenant Improvements**”. Once the Approved Working Drawings have been approved by Landlord and Tenant, Tenant shall make no changes, change orders or modifications thereto without the prior written consent of Landlord, which consent shall not be unreasonably withheld; provided that Landlord may withhold its consent in Landlord’s sole discretion if such change or modification would: (i) be of a quality lower than the quality of the standard tenant improvement items for the Building; and/or (ii) require any changes to the Base, Shell and Core or structural improvements or systems of the Building. The Final Space Plan, Working Drawings and Approved Working Drawings shall be collectively referred to herein as, the “**Construction Drawings**”.

**SECTION 3**

**CONSTRUCTION AND COSTS OF TENANT IMPROVEMENTS**

**3.1 Construction and Cost Proposal.** Landlord shall provide the Construction Drawings to, and solicit construction bids from, not fewer than three (3) qualified and reputable general contractors. The list of bidders shall be determined by Landlord in consultation with Tenant and shall include Landmark Builders (to the extent Landmark Buildings elects to be included in the process). If after receive bids from general contractors Landlord does not wish to award the contract to the lowest bidder among the general contractors who submitted bids, then such decision shall be subject to the approval of Tenant, which approval shall not be unreasonably withheld. Landlord shall cause a contractor designated by Landlord (the “**Contractor**”) to (i) obtain all applicable

**EXHIBIT D**

building permits for construction of the Tenant Improvements (collectively, the “**Permits**”), and (ii) construct the Tenant Improvements as depicted on the Approved Working Drawings, in compliance with such Permits and all applicable laws in effect at the time of construction, and in good workmanlike manner. Landlord shall provide Tenant with a cost proposal in accordance with the Approved Working Drawings (“**Cost Proposal**”). Portions of the cost of the Tenant Improvements may be delivered to Tenant as such portions of the Tenant Improvements are priced by Contractor (on an individual item-by-item or trade-by-trade basis), even before the Approved Working Drawings are completed (the “**Partial Cost Proposal**”). Tenant shall either (a) approve and deliver the Cost Proposal or the Partial Cost Proposal, as applicable to Landlord within five (5) business days of the receipt of the same, or (b) provide proposed “value engineering” to the Cost Proposal or the Partial Cost Proposal, as applicable to Landlord within five (5) business days of the receipt of the Cost Proposal or the Partial Cost Proposal. In the event Tenant shall provide Landlord with its proposed “value engineering”, Landlord shall revise the Cost Proposal or the Partial Cost Proposal, as applicable, and Tenant shall approve same within five (5) business days of the receipt of the revised Cost Proposal or the revised Partial Cost Proposal. The date by which Tenant must approve and deliver the Cost Proposal, or the last Partial Cost Proposal to Landlord, as the case may be, shall be known as the “**Cost Proposal Delivery Date**”. The total of all Partial Cost Proposals, if any, shall be known as the Cost Proposal.

**3.2 Allowance and Over-Allowance Amount.** Landlord shall pay for the cost of the design and construction of the Tenant Improvements in an amount up to, but not exceeding, Fifty-Five Dollars (\$55.00) per rentable square foot of the Premises (i.e., up to Three Million Four Hundred Sixty-Seven Thousand Six Hundred Forty Dollars (\$3,467,640.00) (the “**Allowance**”). The cost of the design and construction of the Tenant Improvements shall include Landlord’s construction supervision and management fee in an amount equal to the product of (i) three percent (3%) and (ii) the total amount of the Allowance and the Over-Allowance Amount (as such term is defined below). On the Cost Proposal Delivery Date, Tenant shall deliver to Landlord cash in an amount (the “**Over-Allowance Amount**”) equal to the difference between (i) the amount of the Cost Proposal and (ii) the amount of the Tenant Improvement Allowance (less any portion thereof already disbursed by Landlord, or in the process of being disbursed by Landlord, on or before the Cost Proposal Delivery Date). The Over Allowance Amount shall be disbursed by Landlord prior to the disbursement of any then remaining portion of the Tenant Improvement Allowance. In the event that after Tenant pays the Over-Allowance Amount, Tenant requests any changes, change orders or modifications to the Final Space Plan (which Landlord approves pursuant to Section 1 above) which increase the cost to construct the Tenant Improvements above the cost of the Tenant Improvements as described in the Final Space Plan (“**Change Orders**”), Tenant shall pay such increased cost to Landlord immediately upon Landlord’s request therefor, and, in any event, prior to the date Landlord causes the Contractor to commence construction of the Change Orders. The cost charged by Landlord to Tenant caused by Tenant’s Change Orders shall be the amount of money Landlord has to pay to cause the Tenant Improvements, as amended by the Change Orders, to be constructed above the costs that Landlord would have had to pay to cause the Tenant Improvements to be constructed if no Change Orders had been made to the Tenant Improvements set forth on the Final Space Plan (“**Differential**”), plus an amount equal to three percent (3%) of the Differential to compensate Landlord for its time and efforts in connection with such Change Orders. If such Change Orders delay Landlord’s completion of the Tenant Improvements set forth on the Final Space Plan, then such delay shall constitute a “**Tenant Delay**”. In no event shall Landlord be obligated to pay for any of Tenant’s furniture, computer systems, telephone systems, equipment or other personal property which may be depicted on the Construction Drawings; such items shall be paid for by Tenant. Tenant shall not be entitled to receive in cash or as a credit against any rental or otherwise, any portion of the Allowance not used to pay for the cost of the design and construction of the Tenant Improvements.

**3.3 Additional Allowance.** In addition to the Allowance, and as a credit against any Over-Allowance Amount payable by Tenant hereunder, Tenant shall be entitled to a one-time additional tenant improvement allowance in an amount up to, but not exceeding, Fifteen Dollars (\$15.00) per rentable square foot of the Premises (i.e., up to Nine Hundred Forty-Five Thousand Seven Hundred Twenty Dollars (\$945,720.00)) (the “**Additional Allowance**”) for the costs of the design and construction of the Tenant Improvements that exceed the amount of the Allowance; provided that the amount of the Additional Allowance so utilized shall be amortized as additional Base Rent payable by Tenant to Landlord over the initial Term (commencing on the Commencement Date) on a straight-line basis at an annual interest rate of eight percent (8%). For avoidance of doubt, the Additional Allowance is not subject to abatement pursuant to Section 4(b) of the Lease.

**3.4 FF&E Allowance.** In addition to the Allowance and the Additional Allowance, Tenant shall be entitled to a one-time FF&E allowance in an amount up to, but not exceeding, Four Dollars (\$4.00) per rentable square foot of the Premises (i.e., up to Two Hundred Fifty-Two Thousand One Hundred Ninety-Two Dollars (\$252,192.00)) (the “**FF&E Allowance**”) for the costs relating to the purchase of Tenant’s furniture, fixtures and equipment within the Premises (“**Tenant’s FF&E**”). Tenant shall not be entitled to receive any cash payment or credit against Rent or otherwise for any portion of the FF&E Allowance which is not used to pay for the Tenant’s FF&E. Tenant shall deliver to Landlord: (i) a request for payment of the FF&E Allowance, in a form to be provided by Landlord, showing the items of Tenant’s FF&E purchased by Tenant and installed in the Premises; (ii) invoices for Tenant’s FF&E purchased by Tenant and installed in the Premises; (iii) executed mechanic’s lien releases from all of Tenant’s agents which shall comply with the appropriate provisions, as reasonably determined by Landlord, of California Civil Code Section 8122 et seq.; and (iv) all other information reasonably

EXHIBIT D

requested by Landlord. Subject to receipt of such deliveries, Landlord shall deliver a check to Tenant made payable to Tenant in the amount so requested, but not exceeding the FF&E Allowance, within thirty (30) days of receipt of such materials.

#### **SECTION 4**

##### **READY FOR OCCUPANCY; SUBSTANTIAL COMPLETION OF THE TENANT IMPROVEMENTS**

**4.1 Ready for Occupancy; Substantial Completion.** For purposes of this Lease, including for purposes of determining the Commencement Date (as set forth in the Basic Lease Information), the Premises shall be “**Ready for Occupancy**” upon Substantial Completion of the Premises. For purposes of this Lease, “**Substantial Completion**” of the Premises shall occur upon the completion of construction of the Tenant Improvements in the Premises pursuant to the Approved Working Drawings, with the exception of any punch list items and any tenant fixtures, work-stations, built-in furniture, or equipment to be installed by Tenant or under the supervision of Contractor.

**4.2 Delay of the Substantial Completion of the Premises.** If there shall be a delay or there are delays in the Substantial Completion of the Premises as a result of any of the following (collectively, “**Tenant Delays**”):

**4.2.1** Tenant’s failure to timely approve the Working Drawings or any other matter requiring Tenant’s approval by the terms of this Work Letter or the Lease;

**4.2.2** a breach by Tenant of the terms of this Work Letter or the Lease;

**4.2.3** Tenant’s request for changes in any of the Construction Drawings and/or any Change Orders;

**4.2.4** Tenant’s requirement for materials, components, finishes or improvements which are not available in a commercially reasonable time given the estimated date of Substantial Completion of the Premises, as set forth in the Lease, or which are different from, or not included in, Landlord’s standard tenant improvement items for the Building;

**4.2.5** changes to the Base, Shell and Core, structural components or structural components or systems of the Building required by the Approved Working Drawings;

**4.2.6** any changes in the Construction Drawings and/or the Tenant Improvements required by applicable laws if such changes are directly attributable to Tenant’s use of the Premises or Tenant’s specialized tenant improvement(s); or

**4.2.7** any other acts or omissions of Tenant, or its agents, or employees; then, notwithstanding anything to the contrary set forth in the Lease and regardless of the actual date of Substantial Completion, the Commencement Date (as set forth in the Basic Lease Information) shall be deemed to be the date the Commencement Date would have occurred if no Tenant Delay or Delays, as set forth above.

#### **SECTION 5**

##### **MISCELLANEOUS**

**5.1 Tenant’s Entry Into the Premises Prior to Substantial Completion.** Subject to the terms hereof and provided that Tenant and its agents do not interfere with Contractor’s work in the Project, the Building and the Premises, at Landlord’s reasonable discretion, Contractor shall allow Tenant access to the Premises at least three (3) weeks prior to the Substantial Completion of the Premises for the purpose of Tenant installing equipment or fixtures (including Tenant’s data and telephone equipment) in the Premises. Prior to Tenant’s entry into the Premises as permitted by the terms of this **Section 5.1**, Tenant shall submit a schedule to Landlord and Contractor, for their approval, which schedule shall detail the timing and purpose of Tenant’s entry. In connection with any such entry, Tenant acknowledges and agrees that Tenant’s employees, agents, contractors, consultants, workmen, mechanics, suppliers and invitees shall fully cooperate, work in harmony and not, in any manner, interfere with Landlord or Landlord’s Contractor, agents or representatives in performing work in the Project, the Building and the Premises, or interfere with the general operation of the Building and/or the Project. If at any time any such person representing Tenant shall not be cooperative or shall otherwise cause or threaten to cause any such disharmony or interference, including, without limitation, labor disharmony, and Tenant fails to immediately institute and maintain corrective actions as directed by Landlord, then Landlord may revoke Tenant’s entry rights

#### **EXHIBIT D**

upon twenty-four (24) hours' prior written notice to Tenant. Tenant acknowledges and agrees that any such entry into and occupancy of the Premises or any portion thereof by Tenant or any person or entity working for or on behalf of Tenant shall be deemed to be subject to all of the terms, covenants, conditions and provisions of the Lease, excluding only the covenant to pay Rent (until the occurrence of the Commencement Date). Tenant further acknowledges and agrees that Landlord shall not be liable for any injury, loss or damage which may occur to any of Tenant's work made in or about the Premises in connection with such entry or to any property placed therein prior to the Commencement Date, the same being at Tenant's sole risk and liability. Tenant shall be liable to Landlord for any damage to any portion of the Premises, including the Tenant Improvement work, caused by Tenant or any of Tenant's employees, agents, contractors, consultants, workmen, mechanics, suppliers and invitees. In the event that the performance of Tenant's work in connection with such entry causes extra costs to be incurred by Landlord, Tenant shall promptly reimburse Landlord for such extra costs and/or shall pay Landlord for such Building services at Landlord's standard rates then in effect. In addition, Tenant shall hold Landlord harmless from and indemnify, protect and defend Landlord against any loss or damage to the Premises or Project and against injury to any persons caused by Tenant's actions pursuant to this [Section 5.1](#).

**5.2 Tenant's Representative.** Tenant has designated Chanterria McGilbra as its sole representative with respect to the matters set forth in this Work Letter, who shall have full authority and responsibility to act on behalf of the Tenant as required in this Work Letter.

**5.3 Landlord's Representative.** Landlord has designated Eric Clapp as its sole representative with respect to the matters set forth in this Work Letter, who, until further notice to Tenant, shall have full authority and responsibility to act on behalf of the Landlord as required in this Work Letter.

**5.4 Time of the Essence in This Work Letter.** Unless otherwise indicated, all references herein to a "number of days" shall mean and refer to calendar days. In all instances where Tenant is required to approve or deliver an item, if no written notice of approval is given or the item is not delivered within the stated time period, at Landlord's sole option, at the end of said period the item shall automatically be deemed approved or delivered by Tenant and the next succeeding time period shall commence.

**5.5 Tenant's Lease Default.** Notwithstanding any provision to the contrary contained in the Lease, if an event of default by Tenant as described in Section 17 of the Lease or any default by Tenant under this Work Letter has occurred at any time on or before the Substantial Completion of the Premises, then (i) in addition to all other rights and remedies granted to Landlord pursuant to the Lease, at law or in equity, Landlord shall have the right to withhold payment of all or any portion of the Allowance and/or Landlord may cause Contractor to cease the construction of the Premises (in which case, Tenant shall be responsible for any delay in the Substantial Completion of the Premises caused by such work stoppage as set forth in Section 5.2 of this Work Letter), and (ii) all other obligations of Landlord under the terms of this Work Letter shall be forgiven until such time as such default is cured pursuant to the terms of the Lease (in which case, Tenant shall be responsible for any delay in Substantial Completion of the Premises caused by such inaction by Landlord). In addition, if the Lease is terminated prior to the Commencement Date, for any reason due to a default by Tenant as described in Section 17 of the Lease or under this Work Letter, in addition to any other remedies available to Landlord under the Lease, at law and/or in equity, Tenant shall pay to Landlord, as Additional Rent under the Lease, within five (5) days of receipt of a statement therefor, any and all costs incurred by Landlord (including any portion of the Allowance disbursed by Landlord) and not reimbursed or otherwise paid by Tenant through the date of such termination in connection with the Tenant Improvements to the extent planned, installed and/or constructed as of such date of termination, including, but not limited to, any costs related to the removal of all or any portion of the Tenant Improvements and restoration costs related thereto.

**5.6 Termination.** Notwithstanding anything in the Lease (including this Work Letter) to the contrary, Tenant acknowledges and agrees that Landlord shall have the right to terminate the Lease by giving Tenant written notice of the exercise of such option (in which event the Lease shall cease and terminate as of the date of such notice) in the event Landlord is unable to obtain the Permits for the Tenant Improvements within one hundred twenty (120) days (as extended for Tenant Delays) from the date of the full execution and delivery of the Lease by Landlord and Tenant. Upon such termination, the parties shall be relieved of all further obligations under the Lease except for those obligations under the Lease which expressly survive the expiration or sooner termination of the Lease.

#### EXHIBIT D

SCHEDULE D-1

DESCRIPTION OF LANDLORD WORK

**ADA Summary:**

The following areas are being upgraded at 5000 Marina to comply with the 2013 CBC accessibility requirements:

- Level 1 restrooms
- Path of travel into the building from the ADA parking spaces at the surface lot
- Rear egress door, egress ramp and associated handrails
- New front entry stairs and ramp and associated handrails
- ADA parking space quantities

**Glazing Summary:**

Replacement windows at Skywall systems

Glass performance characteristics

- U-FACTOR (Insulation Requirement)=0.58
- RSHGC (Reflective Solar Heat Gain Coefficient) =0.41
- VT (Visible Transmittance) =0.46 (Curtain Wall)

**Interior Finishes Summary:**

- All walls to receive new paint
- All existing gypsum board ceiling to be repainted
- Restrooms on levels 1 to receive all new floor and wall finishes
- Lobby to receive new polished concrete flooring
- Elevator frames to be repainted
- Lobby to receive new moss wall installation
- Lobby to receive new composite metal paneling to match exterior canopy
- Exposed concrete on levels 2 and 3
- Existing acoustical ceilings and lighting to remain at the open office

Interior Paint

Manufacturer: Benjamin Moore

Product: Eco Spec N374 and 514 Natura, Zero VOC

Specialty Paint

Manufacturer: Scuffmaster

Product: solid metal paint

Color: SM9740

Restroom Wall Tile

Manufacturer: Daltile

Product: Modern Dimensions

Color 1: Arctic White 0190 Semi-Gloss

Color 2: Arctic White 0790 Matte

SCHEDULE D-1

Restroom Floor Tile  
Manufacturer: Daltile  
Product: Ever, Unpolished  
Color: Artic Ev03  
Size: 12" X 24"

Concrete Micro Topping Finish  
Product: Ardex PC-M Polished Concrete Micro-Topping  
Color: Gray

Concrete Polished  
Product: Concrete Distribution, Inc. Retroplate System

Wood Wall Base  
Manufacturer: Custom paint grade wood  
Color: A92  
Allstate  
Color: A92

Wood Paneling  
Manufacturer: Terramai  
Product: World Mix Paneling Sourced From Reclaimed Cargo Ship Dunnage  
Finish: Clear Poly

Plastic Laminate  
Product: Wilsonart  
Color: D354-60 Designer White

Solid Surface  
Manufacturer: Caesarstone  
Product: 3141 Eggshell

Composite Metal Paneling  
Manufacturer: Citadel  
Product: Envelope 2000  
Color: Series F Charcoal Grey

**Lighting Summary:**

- Lobby to receive all new lighting
- Existing lighting to remain at levels 1-3 open office area
- Existing lighting to remain at restrooms. New vanity lights to be added at level 1 restrooms
- New exterior site lighting to be added building entry

Description: Suspended Led Linear Pendant  
Manufacturer: Vode  
Model: 107-RR-01-4-/-CC-/-/-/-/-Z-SO-35-2-/-AL

Description: Fluorescent Wall Mounted Vanity Light  
Manufacturer: Vode MLR Monopoint Fluorescent, 135 Series Beefuse Rail, Wall Mount  
Model: MLR Monopoint Fluorescent, 135 Series Beefuse Rail, Alum Finish , No Perforated Lens or Baffle

Description: Recessed Led Wallwasher  
Manufacturer: Selux  
Model: M36 LED 1L35-35-A2-/-04-WH

**SCHEDULE D-1**

Description: Recessed Led Linear Downlight  
Manufacturer: Selux  
Model: M36 LED 1L35-35-LW-/-03-WH

Description: Recessed Led Linear Downlight - Exterior  
Manufacturer: Selux  
Model: M36 LED 1L35-35-LW-/-03-SV-/-DL

Description: LED Cove Light  
Manufacturer: Philips  
Model: EW Cove MX Powercore 3500K

Description: Continuous Led Handrail  
Manufacturer: Cooper  
Model: 06-SSS-1-PMC-NR-55-3K

Description: Led Bollard  
Manufacturer: Louis Poulsen  
Model: Flindt-B Natural Al. Finish

Description: LED Inground Uplight  
Manufacturer: B-K Lighting  
Model: Well Star WS-LED-E22-/-WFL-/-/-/-CIF

Description: LED Linear Uplight  
Manufacturer: Beta Calco  
Model: Confine 48 Long LED

Description: Recessed Step Light  
Manufacturer: Beta Calco  
Model: Margin

**HVAC System Summary:**

The HVAC system consist of

- (2) 115 tons Trane rooftop package units.
- Trane Model: SXHGD12, 46,000 CFM, 480V. 3PH, 1,260,000 BTUH COOLING.
- Existing air compressor and pneumatic VAV box system will be replaced with DDC controls VAV system.
- Heating, existing Boiler on roof, 1,825,000 BTUH

**Plumbing System Summary:**

Plumbing system consist of:

Main cold water line is of 3 inches  
Main sewer line is of 6 inches.

- Men's and Women's Restrooms on level 1 to receive all new plumbing fixtures, toilet accessories and vanity counter with mirror

Faucets  
Toto Tel5LI, 0.15 Gallon/Cycle

Lavatory  
Toto LT191, 01 Cotton, Undermount

**SCHEDULE D-1**

Waterclosets

New Sloan Wets-2050-1001 1.28 GPF Wall Mounted Water Closet With Elongated Bowl

Urinals

Sloan Su-1005-0.5 0.5 GPF, Wall Mounted

Toilet Partitions

Hadrian Standard No Sight Line Floor Mounted, Brushed Stainless Steel

Accessories

Bobrick Trimline and Classic Series

**Elevators Summary:**

2 Hydraulic Elevators. Elevators will receive new interior cab finishes, including new aluminum suspended ceiling and LED light fixtures, Aluminum wall panels, Carpet flooring

SCHEDULE D-1

**EXHIBIT E**

**BUILDING RULES AND REGULATIONS**

The following rules and regulations shall apply to the Premises, the Building, the parking area associated therewith, and the appurtenances thereto:

1. Sidewalks, doorways, vestibules, halls, stairways, and other similar areas shall not be obstructed by tenants or used by any tenant for purposes other than ingress and egress to and from their respective leased premises and for going from one to another part of the Building.

2. Plumbing, fixtures and appliances shall be used only for the purposes for which designed, and no sweepings, rubbish, rags or other unsuitable material shall be thrown or deposited therein. Damage resulting to any such fixtures or appliances from misuse by a tenant or its agents, employees or invitees, shall be paid by such tenant.

3. No signs, advertisements or notices (other than those that are not visible outside the Premises) shall be painted or affixed on or to any windows or doors or other part of the Building without the prior written consent of Landlord.

4. Landlord shall provide all door locks in each tenant's leased premises, at the cost of such tenant, and no tenant shall place any additional door locks in its leased premises without Landlord's prior written consent. Landlord shall furnish to each tenant a reasonable number of keys to such tenant's leased premises, at such tenant's cost, and no tenant shall make a duplicate thereof.

5. In connection with the movement in or out of the Building of furniture, fixtures or equipment, or dispatch or receipt by tenants of any bulky material, merchandise or materials, each tenant assumes all risks of and shall be liable for all damage to articles moved and injury to persons or public engaged or not engaged in such movement.

6. Landlord may prescribe weight limitations and determine the locations for safes and other heavy equipment or items, which shall in all cases be placed in the Building so as to distribute weight in a manner reasonably acceptable to Landlord which may include the use of such supporting devices as Landlord may reasonably require. All damages to the Building caused by the installation or removal of any property of a tenant, or done by a tenant's property while in the Building, shall be repaired at the expense of such tenant.

7. No birds or animals (other than seeing-eye dogs) shall be brought into or kept in, on or about any tenant's leased premises. No portion of any tenant's leased premises shall at any time be used or occupied as sleeping or lodging quarters.

8. Tenant shall not make or permit any vibration or improper, objectionable or unpleasant noises (other than such vibrations and noises as are typical for an office building) or odors in the Building or otherwise interfere in any way with other tenants or persons having business with them.

9. No tenant shall use or keep in the Building any flammable or explosive fluid or substance (other than typical office supplies [e.g., photocopier toner] used in compliance with all Laws).

10. Landlord will not be responsible for lost or stolen personal property, money or jewelry from tenant's leased premises or public or common areas regardless of whether such loss occurs when the area is locked against entry or not.

11. No vending or dispensing machines of any kind may be maintained in any leased premises without the prior written permission of Landlord, other than those used for Tenant's employees.

12. Tenant shall not conduct any activity on or about the Premises or Building which will draw pickets, demonstrators, or the like.

13. All vehicles are to be currently licensed, in good operating condition, parked for business purposes having to do with Tenant's business operated in the Premises, parked within designated parking spaces, one vehicle to each space. No vehicles may be stored in the parking areas. No vehicle shall be parked as a "billboard" vehicle in the parking lot. Any vehicle parked improperly may be towed away. Tenant, Tenant's agents, employees, vendors and customers who do not operate or park their vehicles as required shall subject the vehicle to being towed at the expense of the owner or driver. Landlord may place a "boot" on the vehicle to immobilize it and may levy a charge of \$50.00 to remove the "boot."

**EXHIBIT E**

14. No tenant may enter into phone rooms, electrical rooms, mechanical rooms, or other service areas of the Building unless accompanied by Landlord or the Building manager.

15. Tenant shall not permit its employees, invitees or guests to smoke in the Premises, nor shall any tenant permit its employees, invitees, or guests to loiter at the Building entrances for the purposes of smoking. Landlord may, but shall not be required to, designate an area for smoking outside the Building.

16. Canvassing, soliciting or peddling in or about the Premises or the Property is prohibited and Tenant shall cooperate to prevent same.

17. Tenant shall not advertise for temporary laborers giving the Premises or the Project as an address, nor pay such laborers at a location in the Premises or the Project.

18. Tenant shall park trailers and other oversized vehicles only in areas designated by Landlord for the parking of trailers or oversized vehicles. Tenant shall not park trailers and other oversized vehicles in streets or other public areas in the Complex.

19. Tenant shall not utilize the Premises or Project for outside storage except with the written consent of Landlord. The prohibition against outside storage includes, but is not limited to, equipment, materials, vehicles, campers, trailers, boats, barrels, pallets, and trash (other than in containers provided by commercial trash collectors which are picked up on a regularly scheduled basis).

EXHIBIT E

EXHIBIT F

CONFIRMATION OF COMMENCEMENT DATE

\_\_\_\_\_, 2015

Ultragenyx Pharmaceutical Inc.
5000 Marina Boulevard
Brisbane, CA 94005

Re: Lease Agreement (the "Lease") dated \_\_\_\_\_, 2015, between MARINA BOULEVARD PROPERTY, LLC, a Delaware limited liability company ("Landlord"), and ULTRAGENYX PHARMACEUTICAL INC., a Delaware corporation ("Tenant"). Capitalized terms used herein but not defined shall be given the meanings assigned to them in the Lease.

Ladies and Gentlemen:

Landlord and Tenant agree as follows:

1. Condition of Premises. Tenant has accepted possession of the Premises pursuant to the Lease. Any improvements required by the terms of the Lease to be made by Landlord have been completed to the full and complete satisfaction of Tenant in all respects. Furthermore, Tenant acknowledges that the Premises are suitable for the Permitted Use.

2. Commencement Date. The Commencement Date of the Lease is \_\_\_\_\_, 20\_\_.

3. Expiration Date. The Term is scheduled to expire on the last day of the one hundred twenty-second (122nd) full calendar month of the Term, which date is \_\_\_\_\_, 20\_\_.

4. Contact Person. Tenant's contact person in the Premises is:

Ultragenyx Pharmaceutical Inc.
5000 Marina Boulevard
Brisbane, CA 94005
Attention: \_\_\_\_\_
Telephone: \_\_\_\_\_
Telecopy: \_\_\_\_\_

5. Base Rent. Base Rent shall be payable monthly in advance in accordance with the following schedule:

Table with 4 columns: Lease Month, Annual Base Rent, Monthly Base Rent, Monthly Rental Rate Per RSF. Rows include lease months from 1-12\* to 121-122 with corresponding rent values.

6. Ratification. Tenant hereby ratifies and confirms its obligations under the Lease, and represents and warrants to Landlord that it has no defenses thereto. Additionally, Tenant further confirms and ratifies that, as of the date hereof, (a) the Lease is and remains in good standing and in full force and effect, and (b) Tenant has no claims, counterclaims, set-offs or defenses against Landlord arising out of the Lease or in any way relating thereto or arising out of any other transaction between Landlord and Tenant.

EXHIBIT F

7. Binding Effect; Governing Law. Except as modified hereby, the Lease shall remain in full effect and this letter shall be binding upon Landlord and Tenant and their respective successors and assigns. If any inconsistency exists or arises between the terms of this letter and the terms of the Lease, the terms of this letter shall prevail. This letter shall be governed by the laws of the state in which the Premises are located.

Please indicate your agreement to the above matters by signing this letter in the space indicated below and returning an executed original to us.

Sincerely,

MARINA LANDING PROPERTY, LLC,  
a Delaware limited liability company

By: \_\_\_\_\_  
Printed Name: \_\_\_\_\_  
Title: \_\_\_\_\_

By: \_\_\_\_\_  
Printed Name: \_\_\_\_\_  
Title: \_\_\_\_\_

Agreed and accepted:

ULTRAGENYX PHARMACEUTICAL INC.,  
a Delaware corporation

By: \_\_\_\_\_  
Printed Name: \_\_\_\_\_  
Title: \_\_\_\_\_

By: \_\_\_\_\_  
Printed Name: \_\_\_\_\_  
Title: \_\_\_\_\_

EXHIBIT F

EXHIBIT G

**FORM OF TENANT ESTOPPEL CERTIFICATE**

The undersigned is the Tenant under the Lease (defined below) between \_\_\_\_\_, a \_\_\_\_\_, as Landlord, and the undersigned as Tenant, for the Premises on the \_\_\_\_\_ floor(s) of the office building located at \_\_\_\_\_, \_\_\_\_\_ and commonly known as \_\_\_\_\_, and hereby certifies as follows:

1. The Lease consists of the original Lease Agreement dated as of \_\_\_\_\_, 20\_\_ between Tenant and Landlord [‘s predecessor-in-interest] and the following amendments or modifications thereto (if none, please state “none”): \_\_\_\_\_

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The documents listed above are herein collectively referred to as the “Lease” and represent the entire agreement between the parties with respect to the Premises. All capitalized terms used herein but not defined shall be given the meaning assigned to them in the Lease.

2. The Lease is in full force and effect and has not been modified, supplemented or amended in any way except as provided in Section 1 above.

3. The Term commenced on \_\_\_\_\_, 20\_\_, and the Term expires, excluding any renewal options, on \_\_\_\_\_, 20\_\_, and Tenant has no option to purchase all or any part of the Premises or the Building or, except as expressly set forth in the Lease, any option to terminate or cancel the Lease.

4. Tenant currently occupies the Premises described in the Lease and Tenant has not transferred, assigned, or sublet any portion of the Premises nor entered into any license or concession agreements with respect thereto except as follows (if none, please state “none”):

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5. All monthly installments of Base Rent, all Additional Rent and all monthly installments of estimated Additional Rent have been paid when due through \_\_\_\_\_. The current monthly installment of Base Rent is \$\_\_\_\_\_.

6. All conditions of the Lease to be performed by Landlord necessary to the enforceability of the Lease have been satisfied and Landlord is not in default thereunder. In addition, Tenant has not delivered any notice to Landlord regarding a default by Landlord thereunder.

7. As of the date hereof, there are no existing defenses or offsets, or, to the undersigned’s knowledge, claims or any basis for a claim, that the undersigned has against Landlord and no event has occurred and no condition exists, which, with the giving of notice or the passage of time, or both, will constitute a default under the Lease.

8. No rental has been paid more than thirty (30) days in advance and no security deposit has been delivered to Landlord except as provided in the Lease.

9. If Tenant is a corporation, partnership or other business entity, each individual executing this Estoppel Certificate on behalf of Tenant hereby represents and warrants that Tenant is a duly formed and existing entity qualified to do business in the state in which the Premises are located and that Tenant has full right and authority to execute and deliver this Estoppel Certificate and that each person signing on behalf of Tenant is authorized to do so.

10. There are no actions pending against Tenant under any bankruptcy or similar laws of the United States or any state.

11. Other than as approved by Landlord in writing and used in compliance with all applicable laws and incidental to the ordinary course of the use of the Premises, the undersigned has not used or stored any hazardous substances in the Premises.

EXHIBIT G

12. All tenant improvement work to be performed by Landlord under the Lease has been completed in accordance with the Lease and has been accepted by the undersigned and all reimbursements and allowances due to the undersigned under the Lease in connection with any tenant improvement work have been paid in full.

Tenant acknowledges that this Estoppel Certificate may be delivered to Landlord, Landlord's Mortgagee or to a prospective mortgagee or prospective purchaser, and their respective successors and assigns, and acknowledges that Landlord, Landlord's Mortgagee and/or such prospective mortgagee or prospective purchaser will be relying upon the statements contained herein in disbursing loan advances or making a new loan or acquiring the property of which the Premises are a part and that receipt by it of this certificate is a condition of disbursing loan advances or making such loan or acquiring such property.

Executed as of \_\_\_\_\_, 20\_\_.

**TENANT:**

\_\_\_\_\_

a

\_\_\_\_\_

By: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

EXHIBIT G

**EXHIBIT H**

**RENEWAL OPTION**

Provided that an uncured Event of Default does not exist at the time of such election and at any time prior to the commencement of the extended Term and Tenant is then occupying not less than fifty percent (50%) of the Premises at the time of such election, Tenant may renew this Lease for two (2) additional period(s) of five (5) years each, by delivering written notice of the exercise thereof to Landlord not earlier than fifteen (15) months nor later than twelve (12) months before the expiration of the then-current Term ("**Tenant's Election Notice**"). The Base Rent payable for each month during such extended Term shall be equal to the prevailing rental rate (the "**Prevailing Rental Rate**"), at the commencement of such extended Term, for renewals of space in the Complex and in comparable buildings located within North San Mateo County, California, of equivalent quality, size, utility and location, with the length of the extended Term and the credit standing of Tenant, and the tenant improvement allowance and other tenant concessions to be provided (or not provided) to be taken into account. Within fifteen (15) days after receipt of Tenant's notice to renew, Landlord shall deliver to Tenant written notice of the Prevailing Rental Rate and shall advise Tenant of the required adjustment to Base Rent, if any, and the other terms and conditions offered. Tenant shall, within ten (10) days after receipt of Landlord's notice, notify Landlord in writing whether Tenant accepts or rejects Landlord's determination of the Prevailing Rental Rate. If Tenant timely notifies Landlord that Tenant accepts Landlord's determination of the Prevailing Rental Rate, then, on or before the commencement date of the extended Term, Landlord and Tenant shall execute an amendment to this Lease extending the Term on the same terms provided in this Lease, except as follows:

- (a) Base Rent shall be adjusted to the Prevailing Rental Rate;
- (b) Tenant shall have no further renewal option unless expressly granted by Landlord in writing; and
- (c) Landlord shall lease to Tenant the Premises in their then-current condition, and Landlord shall not provide to Tenant any allowances (e.g., moving allowance, construction allowance, and the like) or other tenant inducements.

If by the date thirty (30) days following delivery of Tenant's Election Notice, Landlord and Tenant have not agreed in writing as to the amount of the Base Rent, the parties shall determine the projected Prevailing Rental Rate in accordance with the following procedure (which procedure is herein referred to as the "**Three-Appraiser Method**"). Landlord and Tenant shall each appoint one (1) real estate appraiser, and the two (2) so appointed shall select a third. Said real estate appraisers shall each be licensed in the state in which the Premises is located, specializing in the field of commercial real estate in North San Mateo County, California, having no less than ten (10) years' experience in such field, unaffiliated with either Landlord or Tenant and recognized as ethical and reputable within their field. Landlord and Tenant agree to make their appointments promptly within ten (10) days after expiration of the thirty (30) day negotiation period, or sooner if mutually agreed upon. The two (2) appraisers selected by Landlord and Tenant shall promptly select a third appraiser within fifteen (15) days after they both have been appointed, and each appraiser, within fifteen (15) days after the third appraiser is selected, shall submit his or her determination of the then projected Prevailing Rental Rate. The Prevailing Rental Rate shall be the mean of the two (2) closest rental determinations. If either Landlord or Tenant fails to appoint an appraiser within the time period specified in this paragraph, the appraiser appointed by one of them shall reach a decision, notify Landlord and Tenant thereof, and such appraiser's decision shall be binding upon Landlord and Tenant. Each party shall pay the fees and expenses of the appraiser appointed by or on behalf of it, and each shall pay one-half of the fees and expenses of the third appraiser.

Tenant shall confirm Tenant's acceptance of the determination of the Prevailing Rental Rate by executing an amendment to this Lease memorializing the same within ten (10) days of such determination (herein the "**Extension Amendment**"). Tenant's failure to execute and deliver the Extension Amendment to Landlord within such 10-day period shall be deemed to be Tenant's election not to extend the Term of this Lease in which event the provisions of this Exhibit H shall have no further force or effect, Tenant shall have no right to renew this Lease and the Term of this Lease shall terminate upon the expiration date of the then-current Term.

Notwithstanding anything in the foregoing to the contrary, at Landlord's option, and in addition to all of Landlord's remedies under this Lease, at law or in equity, the right to extend the Term of this Lease hereinabove granted to Tenant shall not be deemed to be properly exercised if, as of the date Tenant exercises its extension right or on the scheduled commencement date for the applicable option term, Tenant is in default under this Lease beyond any applicable notice and cure period. Further, Tenant's rights under this Exhibit shall terminate if (1) this Lease or Tenant's right to possession of the Premises is terminated, (2) Tenant fails to timely exercise its option under this Exhibit, time being of the essence with respect to Tenant's exercise thereof, or (3) Tenant assigns any of its interest in this Lease or sublets any portion of the Premises to any party other than a Permitted Transferee.

**EXHIBIT H**

**EXHIBIT I**

**CONTRACTOR INSURANCE REQUIREMENTS**

**CONTRACTOR INSURANCE REQUIREMENTS**

Contractor shall procure and maintain in effect during the term of the contract the insurance coverage's described, which insurance shall be placed with insurance companies approved by Owner and having a general policyholders' rating of not less than "A" and a financial rating of not less than "8" or better by the latest issue of Best's Key Rating Guide. Such insurance companies shall be licensed and authorized to do business in the jurisdiction in which the Property is located.

Contractor, at its sole cost and expense, shall procure and maintain the following policies of insurance:

- A. **Worker's Compensation Insurance** with statutory benefits and limits which shall fully comply with all applicable state and federal requirements and which shall also include Broad Form All States and Voluntary Compensation Endorsements and Employer's Liability Insurance with limits of not less than \$1,000,000 per accident, \$1,000,000 per disease, and a \$2,000,000 policy limit.
- B. **Automobile Liability Insurance** in Contractor's name covering all owned, non-owned, leased and hired vehicles utilized by Contractor, with a combined single limit per occurrence for bodily injury and property damage of not less than \$1,000,000.
- C. **Commercial General Liability Insurance** on an occurrence basis in Contractor's name, providing coverage of not less than \$2,000,000 per occurrence, which shall include: Bodily Injury, Personal Injury, Products and Completed Operations (for a minimum of two (2) years after final acceptance), Blanket Contractual Liability and Broad Form Property Damage coverage, with bodily injury and property damage of combined single limits of not less than \$2,000,000 per occurrence. The required policy shall not contain any limitation of coverage and/or exclusion coverage for Explosion, Collapse and Underground Hazards (X, C, U). Contractor may provide the coverage required herein through the use of a primary liability policy and umbrella liability policies.
- D. **Additional Insured's**: Contractor shall add Owner, Manager and Associates as additional insured's to Contractor's Liability Policy.

Contractor agrees with respect to all insurance provided or required (except Worker's Compensation and Professional Liability coverage) to require each policy (through endorsement or otherwise) to contain the following wording:

"It is agreed that the 'Person Insured' provision of this policy is amended to include, **Marina Boulevard Property, LLC, Westport Capital Partners, LLC, Sentinel Development Services, Inc. dba: Sentinel Property Services, Sentinel Development Services, Inc. dba: Sentinel Development, Sentinel Development Services, Inc.** and their officers, directors, shareholders and employees as **Additional Insured**, jointly and severally, with respect to any coverage afforded by this policy, but only with respect to operations by, or on behalf of, or to facilities of, used by, or for, the Named Insured. It is further agreed that this insurance shall not be prejudiced as to these Additional Insured by any act or negligence, error or omission of the Named Insured as respects payment of premium, reporting of claims, or any other duties required of the Named Insured by the policy."

All Certificates of Insurance and all notices required shall be sent to:

**MARINA BOULEVARD PROPERTY, LLC**  
**c/o Sentinel Property Services**  
**18301 Von Karman, Suite 510**  
**Irvine, CA 92612**  
**FAX: (949) 582-1339**  
**PHONE: (949) 582-1948**

**EXHIBIT I**

EXHIBIT J

ENVIRONMENTAL QUESTIONNAIRE AND DISCLOSURE STATEMENT

The purpose of this form is to obtain information regarding the use of hazardous substances on the Premises. Tenant should answer the questions as they relate to proposed operations on the Premises and should update any information previously submitted. If additional space is needed to answer the questions, you may attach separate sheets of paper to this form.

**1. GENERAL INFORMATION**

Name of Responding Company: \_\_\_\_\_

Check the Applicable Status:

Prospective Tenant \_\_\_\_ Existing Tenant \_\_\_\_

Mailing Address: \_\_\_\_\_

Contact Person and Title: \_\_\_\_\_

Telephone Number: (\_\_\_\_) \_\_\_\_\_

Address of Premises: \_\_\_\_\_

Length of Lease Term: \_\_\_\_ years with \_\_\_\_ \_\_\_\_ year extension options

Describe the proposed operations to take place on the Premises, including principal products manufactured or services to be conducted.

\_\_\_\_\_

**2. STORAGE OF HAZARDOUS MATERIALS**

2.1 Will any hazardous materials be used or stored on-site?

Wastes Yes \_\_\_\_ No \_\_\_\_  
Chemical Products Yes \_\_\_\_ No \_\_\_\_

2.2 Attach the list of any hazardous materials to be used or stored, the quantities that will be on-site at any time, and the location and method of storage (e.g., 55 gallon drums on concrete pad).

**3. STORAGE TANKS & SUMPS**

3.1 Is any above or below ground storage of gasoline, diesel, or other hazardous substances in tanks or sumps proposed or currently conducted on the Premises?

Yes \_\_\_\_ No \_\_\_\_

If yes, describe the materials to be stored, and the type, size and construction of the sump or tank. Attach copies of any permits obtained for the storage of such substances.

3.2 Have any of the tanks or sumps been inspected or tested for leakage?

Yes \_\_\_\_ No \_\_\_\_

If so, attach the results.

EXHIBIT J

\_\_\_\_\_

3.3 Have any spills or leaks occurred from such tanks or sumps?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, describe.

3.4 Were any regulatory agencies required to be notified of the spill or leak and did such required notification occur?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, attach copies of any spill reports filed, any clearance letters or other correspondence from regulatory agencies relating to the spill or leak.

3.5 Have any underground storage tanks or sumps been taken out of service or removed?

Yes \_\_\_\_\_ No \_\_\_\_\_

If yes, attach copies of any closure permits and clearance obtained from regulatory agencies relating to closure and removal of such tanks.

#### 4. SPILLS

4.1 During the past year, have any spills occurred on the Premises?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, please describe the spill and attach the results of any testing conducted to determine the extent of such spills.

4.2 Were any agencies required to be notified in connection with such spills and did such notification occur?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, attach copies of any spill reports or other correspondence with regulatory agencies.

4.3 Were any clean-up actions undertaken in connection with the spills?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, briefly describe the actions taken. Attach copies of any clearance letters obtained from any regulatory agencies involved and the results of any final soil or groundwater sampling done upon completion of the clean-up work.

#### 5. WASTE MANAGEMENT

5.1 Has your company been issued an EPA or state Hazardous Waste Generator I.D. Number?

Yes \_\_\_\_\_ No \_\_\_\_\_

5.2 Has your company filed any required report as a hazardous waste generator?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, attach a copy of the most recent report filed.

5.3 Attach the list of the hazardous waste, if any, generated or to be generated at the Premises, its hazard class and the quantity generated on a monthly basis.

EXHIBIT J

5.4 Describe the method(s) of disposal for each waste. Indicate where and how often disposal will take place.

\_\_\_\_\_.

5.5 Indicate the name of the person(s) responsible for maintaining copies of hazardous waste manifests completed for off-site shipments of hazardous waste. \_\_\_\_\_

5.6 Is any treatment or processing of hazardous wastes currently conducted or proposed to be conducted at the Premises:

Yes \_\_\_\_\_ No \_\_\_\_\_

If yes, please describe any existing or proposed treatment methods. \_\_\_\_\_

Attach copies of any hazardous waste permits or licenses issued to your company with respect to its operations on the Premises.

\_\_\_\_\_

**6. WASTEWATER TREATMENT/DISCHARGE**

6.1 Do you discharge wastewater to:

\_\_\_\_\_ storm drain? \_\_\_\_\_ sewer?  
\_\_\_\_\_ surface water? \_\_\_\_\_ no industrial discharge

6.2 Is your wastewater treated before discharge?

Yes \_\_\_\_\_ No \_\_\_\_\_

If yes, describe the type of treatment conducted. \_\_\_\_\_

6.3 Attach copies of any wastewater discharge permits issued to your company with respect to its operations on the Premises.

\_\_\_\_\_.

**7. AIR DISCHARGES**

7.1 Do you have any air filtration systems or stacks that discharge into the air?

Yes \_\_\_\_\_ No \_\_\_\_\_

7.2 Do you operate any of the following types of equipment, or any other equipment requiring an air emissions permit?

\_\_\_\_\_ Spray booth  
\_\_\_\_\_ Dip tank  
\_\_\_\_\_ Drying oven  
\_\_\_\_\_ Incinerator  
\_\_\_\_\_ Other (Please Describe)  
\_\_\_\_\_ No Equipment Requiring Air Permits

7.3 Are air emissions from your operations monitored?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, indicate the frequency of monitoring and a description of the monitoring results. \_\_\_\_\_

Attach copies of any air emissions permits pertaining to your operations on the Premises. \_\_\_\_\_

EXHIBIT J

\_\_\_\_\_

**8. HAZARDOUS MATERIALS DISCLOSURES**

8.1 Does your company handle hazardous materials in a quantity equal to or exceeding an aggregate of 500 pounds, 55 gallons, or 200 cubic feet?

Yes \_\_\_\_\_ No \_\_\_\_\_

8.2 Has your company prepared a hazardous materials management plan (“business plan”) pursuant to County Fire Department requirements?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, attach a copy of the business plan.

8.3 Describe the procedures followed to comply with OSHA Hazard Communication Standard requirements.

\_\_\_\_\_.

**9. ENFORCEMENT ACTIONS, COMPLAINTS**

9.1 Has your company even been subject to any agency enforcement actions, administrative orders, or consent decrees?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, describe the actions and any continuing compliance obligations imposed as a result of these actions.

9.2 Has your company even received requests for information, notice or demand letters, or any other inquiries regarding its operations?

Yes \_\_\_\_\_ No \_\_\_\_\_

9.3 Have there ever been, or are there now pending, any lawsuits against the company regarding any environmental or health and safety concerns?

Yes \_\_\_\_\_ No \_\_\_\_\_

9.4 Has an environmental audit even been conducted at your company’s current facility?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, discuss the results of the audit. \_\_\_\_\_

9.5 Have there been any problems or complaints from neighbors at the company’s current facility?

Yes \_\_\_\_\_ No \_\_\_\_\_

If so, describe the problems or complaints. \_\_\_\_\_

Company \_\_\_\_\_

By: \_\_\_\_\_

Title: \_\_\_\_\_

Date: \_\_\_\_\_

EXHIBIT J

**Environmental Questionnaire**

**LIST OF HAZARDOUS MATERIALS TO BE USED OR STORED ON THE PREMISES**

Tenant's operations within the Premises will utilize the following Hazardous Materials:

[LIST HERE]

EXHIBIT J

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**EXHIBIT K**

**BUILDING STANDARDS**

**5000 & 7000 Marina Blvd Interior Finish Specifications**

- Flooring
  - Carpet – All enclosed offices and under workstations to have Carpet tile and 4” rubber base.
  - Concrete – All main paths of travel, kitchen spaces and open areas to have abraded concrete finish. Patch and repair any divots, gouges or imperfections greater than at ¼” diameter
  - Tiling – Restroom tile to match existing first floor tile.
- Partitions
  - Framed partitions to be 18 ga studs with insulation, full height at meeting rooms and executive offices. All other to extend 12” above grid.
- Glass & Glazing
  - Wilson Partitions (or equal) standard clear anodized frame interior storefront to 8’0” where shown.
- Doors & Hardware
  - At meeting rooms, executive offices, training rooms and kitchen areas: Solid core stain or paint grade doors, drop seal and clear anodized frame.
  - Hardware to be brushed aluminum or nickel.
- Acoustical Ceiling
  - Armstrong Optima 2’x2’ or 2’x4’ lay in tiles (or equal)
- Window shades
  - Mecco style roller shade (or equal) at all perimeter windows.

**EXHIBIT K**

## Subsidiaries of Ultragenyx Pharmaceutical Inc.

Name of Subsidiary	Jurisdiction of Incorporation
Ultragenyx UK Ltd	United Kingdom
Ultragenyx International Ltd.	Cayman Islands
Ultragenyx International UX001 Ltd.	Cayman Islands
Ultragenyx International UX003 Ltd.	Cayman Islands
Ultragenyx International UX007 Ltd.	Cayman Islands
Ultragenyx International UX023 Ltd.	Cayman Islands

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in the following Registration Statements:

- (1) Registration Statement (Form S-3 No. 333-201838) of Ultragenyx Pharmaceutical Inc., and
- (2) Registration Statement (Form S-8 Nos. 333-201843 and 333-194773) pertaining to the 2011 Equity Incentive Plan, as amended, 2014 Incentive Plan and 2014 Employee Stock Purchase Plan of Ultragenyx Pharmaceutical Inc.;

of our reports dated February 25, 2016, with respect to the consolidated financial statements of Ultragenyx Pharmaceutical Inc. and the effectiveness of internal control over financial reporting of Ultragenyx Pharmaceutical Inc. included in this Annual Report (Form 10-K) of Ultragenyx Pharmaceutical Inc. for the year ended December 31, 2015.

/S/ ERNST & YOUNG LLP

Redwood City, California

February 25, 2016

## CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Emil D. Kakkis, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ultragenyx Pharmaceutical Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's Board of Directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: February 25, 2016

/s/ Emil D Kakkis

Emil D. Kakkis, M.D., Ph.D.  
President and Chief Executive Officer  
(Principal Executive Officer)

## CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Shalini Sharp, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ultragenyx Pharmaceutical Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's Board of Directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: February 25, 2016

/s/ Shalini Sharp

Shalini Sharp  
Chief Financial Officer and Senior Vice President  
(Principal Financial Officer)

**CERTIFICATION PURSUANT TO SECTION 906 OF  
THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. SECTION 1350)**

In connection with the accompanying Quarterly Report of Ultragenyx Pharmaceutical Inc. (the "Company") on Form 10-K for the year ended December 31, 2015 (the "Report"), I, Emil D. Kakkis, M.D., Ph.D., as President and Chief Executive Officer of the Company, and Shalini Sharp, as Chief Financial Officer and Senior Vice President of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: February 25, 2016

/s/ Emil D. Kakkis  
Emil D. Kakkis, M.D., Ph.D.  
President and Chief Executive Officer  
(Principal Executive Officer)

Dated: February 25, 2016

/s/ Shalini Sharp  
Shalini Sharp  
Chief Financial Officer and Senior Vice President  
(Principal Financial Officer)