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, 2019

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	**27-2546083**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
60 Leveroni Court **Novato, California**	**94949**
(Address of principal executive offices)	*(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	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.001 par value	**RARE**	**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 every Interactive Data File required to be submitted 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 such files). YES ☑ NO ☐

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

Large accelerated filer ☑ Accelerated filer ☐
Non- accelerated filer ☐ Smaller reporting company ☐
Emerging growth company ☐

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

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, 2019 was approximately $2.7 billion, based upon the closing price on The Nasdaq Global Select Market reported for such date. Shares of common stock held by each executive 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 10, 2020, the Company had 57,888,859 shares of common stock issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2020 Annual Meeting of Stockholders, to be held on or about June 26, 2020, 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

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words, or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our commercialization, marketing, and manufacturing capabilities and strategy;
- our expectations regarding the timing of clinical study commencements and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the anticipated indications for our product candidates, if approved;
- the potential market opportunities for commercializing our products and product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our products and product candidates, if approved for commercial use;
- estimates of our expenses, revenue, capital requirements, and our needs for additional financing;
- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business, products and product candidates and the integration and performance of any businesses we have acquired or may acquire;
- the initiation, timing, progress, and results of ongoing and future preclinical and clinical studies, and our research and development programs;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and product candidates;
- our ability to maintain and establish collaborations or strategic relationships or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- our financial performance and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- developments and projections relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part I, Item 1A. Risk Factors.

Any forward-looking statements in this Annual Report reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those discussed under Part I, Item 1A. Risk Factors and discussed elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report 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.

As used in this Annual Report, “Ultragenyx,” “we,” “our,” and similar terms include Ultragenyx Pharmaceutical Inc. and its subsidiaries, unless the context indicates otherwise.

PART I

Item 1. *Business*

Overview

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

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

We were founded in April 2010 by our current President and Chief Executive Officer, Emil Kakkis, M.D., Ph.D., and we have since assembled an experienced team with extensive rare disease drug development and commercialization capabilities.

Our Strategy

The critical components of our business strategy include the following:

- ***Focus on rare and ultra-rare genetic diseases with significant unmet medical need and clear biology.*** There are numerous rare and ultra-rare genetic diseases that currently have no drug therapy approved that treat the underlying disease. Patients suffering from these diseases often have a significant morbidity and/or mortality. We focus 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. We believe that developing drugs that directly impact known disease pathways will increase the probability of success of our development programs. Our modalities of small molecules, biologics, gene therapy, and nucleic acids provide us with what we believe is an optimal set of options to treat metabolic genetic diseases by selecting the best treatment strategy available for each disease.
- ***In-license promising product candidates; retain global commercialization rights to product candidates.*** Our current product candidates are generally in-licensed from academic institutions or derived from partnerships with other pharmaceutical companies. We believe parties agree to license product candidates to us because they are confident in our team's expertise in rare disease drug development and commercialization. We generally intend to retain global commercialization rights to our products and product candidates whenever possible to maximize the potential value of our product portfolio. We do not currently intend to invest significant 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. Because rare disease programs involve fewer patients and may have accelerated paths to market, we are able to feasibly develop multiple clinical-stage product candidates in parallel, resulting in a more diversified portfolio that provides multiple opportunities to create value, with some economies of scale.
- ***Commercialize through patient-focused global organization.*** We seek to commercialize our products in North America, the European Union, or EU, and United Kingdom, Latin America, and select international markets. We have established our own commercial organization in these markets and a network of third-party distributors in smaller markets. We believe our commercial organization is highly specialized and focused, due to the nature of rare disease treatment. In the United States, we have a team of patient diagnosis liaisons who are responsible for finding new doctors with patients with the disease, a separate team of UltraCare Liaisons who assist physicians in placing patients on therapy, and UltraCare Guides who support patients and their families with treatment or reimbursement needs. In addition, we offer a free drug program for patients who are actively navigating the reimbursement process.

Approved Products and Clinical Product Candidates

Our current approved products and clinical-stage pipeline consist of three product categories: biologics, small molecules, and gene therapy product candidates.

We have two commercially approved products, Crysvita® (burosumab) for the treatment of X-linked hypophosphatemia, or XLH, and Mepsevii® (vestronidase alfa) for the treatment of mucopolysaccharidosis VII, or MPSVII or Sly Syndrome, and three additional product candidates in the clinical pipeline. The following table summarizes our approved products and clinical product candidate pipeline:

Approved Products

Crysvita for the treatment of XLH

Crysvita is an antibody administered via subcutaneous injection that targets fibroblast growth factor 23, or FGF23, developed for the treatment of XLH, a rare, hereditary, progressive and lifelong musculoskeletal disorder characterized by renal phosphate wasting caused by excess FGF23 production. There are approximately 48,000 patients with XLH in the developed world, including approximately 36,000 adults and 12,000 children. Crysvita is the only approved treatment that addresses the underlying cause of XLH. Crysvita is approved in the United States for the treatment of XLH in adult and pediatric patients six months of age and older, and in Canada for the treatment of XLH in adult and pediatric patients one year of age and older. In the European Union, or the EU, and the United Kingdom, Crysvita is conditionally approved for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing skeletons. A filing to expand the label to include adults with XLH was submitted in November 2019 by our partner, Kyowa Kirin International, or Kyowa Kirin, in the EU and the United Kingdom. In Brazil, Crysvita is approved for treatment of XLH in adult and pediatric patients one year of age and older. We have submitted regulatory filings in various other Latin American countries.

We are collaborating with Kyowa Kirin Co., Ltd., or KKC (formerly Kyowa Hakko Kirin Co., Ltd., or KHK), and Kyowa Kirin, a wholly owned subsidiary of KKC, on the development and commercialization of Crysvita globally.

In September 2019, we announced that the U.S. Food and Drug Administration, or FDA, approved a label expansion for Crysvita. The label was updated to include new clinical data demonstrating superiority of treatment with Crysvita versus oral phosphate and active vitamin D (conventional therapy) in pediatric patients with XLH, and improvement in stiffness and maintenance of efficacy of Crysvita in adult patients with longer-term treatment. The indication was also expanded to include infants as young as six months of age.

In December 2019, we sold to Royalty Pharma for $320.0 million our royalty interest in Crysvita in the European territory (defined below), where it is being commercialized by KKC.

Mepsevii for the treatment of MPS VII

Mepsevii is an intravenous, or IV, enzyme replacement therapy, developed for the treatment of Mucopolysaccharidosis VII, also known as MPS VII or Sly syndrome, a rare lysosomal storage disease that often leads to multi-organ dysfunction, pervasive skeletal disease, and death. MPS VII is one of the rarest MPS disorders, affecting an estimated 200 patients in the developed world. Mepsevii is approved in the United States for the treatment of children and adults with MPS VII. In the EU and the United Kingdom, Mepsevii

is approved under exceptional circumstances for the treatment of non-neurological manifestations of MPS VII for patients of all ages. In Brazil, Mepsevii is approved for the treatment of MPS VII for patients of all ages

Please see "—License and Collaboration Agreements—Approved Products—Saint Louis University" for a description of our license agreement with Saint Louis University.

Clinical Product Candidates

Crysvita for the treatment of tumor-induced osteomalacia, or TIO

We are also developing Crysvita for the treatment of 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. There are approximately 2,000 to 4,000 patients with TIO in the developed world.

In October 2018, we presented positive 48-week and 72-week data from an ongoing Phase 2 study of Crysvita in adults with TIO syndrome at the American Society for Bone and Mineral Research 2018 Annual Meeting in Montreal. In adults with TIO, Crysvita was associated with increases in serum phosphorous and 1,25(OH)2D; improvement in osteomalacia; improvement in mobility and vitality; and reductions in fatigue.

In December 2019, we submitted an sBLA to the FDA for Crysvita for the treatment of FGF23-related hypophosphatemia associated with phosphaturic mesenchymal tumors, or tumor-induced osteomalacia or TIO, which cannot be curatively resected or localized. We expect to hear back from FDA on submission acceptance and review designation in February 2020.

Please see "—License and Collaboration Agreements—Approved Products—Kyowa Hakko Kirin" for a description of our collaboration and license agreement with KKC.

UX007 for the treatment of Long Chain Fatty-Acid Oxidation Disorders, or LC-FAOD

UX007 is a synthetic triglyceride with a specifically designed chemical composition being studied for the treatment of LC-FAOD, which is a set of rare metabolic diseases that prevents the conversion of fat into energy and can cause low blood sugar, muscle rupture, and heart and liver disease. 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 management with the current standard of care, many patients continue to suffer significant morbidities and mortality. There are approximately 8,000 to 14,000 patients in the developed world with LC-FAOD.

In January 2019, we announced positive topline data from the ongoing long-term extension study of UX007 in patients with LC-FAOD, demonstrating sustained reductions in the duration and frequency of MCEs and a long-term safety profile similar to what has previously been seen with UX007. A total of 75 patients are enrolled in the study including 24 patients who were previously enrolled in the company-sponsored Phase 2 study, 20 naïve patients who had not previously been treated with UX007 and 31 patients from expanded access or investigator-sponsored studies. Patients who previously completed the Phase 2 company-sponsored study and rolled over to the extension study received treatment for an additional 78 weeks. The median annualized MCE and duration rates during the extension treatment period were zero. Over the entire treatment period, patients had a 67 percent reduction in median annualized event rate and a 66 percent reduction in the median annualized duration rate. Patients who were naïve to UX007 at study entry have received up to 78 weeks of treatment. These patients have demonstrated a 70 percent reduction in the median annualized event rate (2.3 events/year pre-UX007 to 0.7 events/year during extension study treatment period) and an 80 percent reduction in the median annualized duration rate (10.0 days/year pre-UX007 treatment to 2.0 days/year during extension study treatment period). Overall, the safety profile observed in the long-term extension study was consistent with what has been previously observed with UX007. The most common treatment-related adverse events were diarrhea, vomiting, and abdominal pain. One patient discontinued due to a treatment-related adverse event. There were two deaths during the extension study, both deemed to be related to disease progression and not due to treatment with UX007. One of these patients was naïve to UX007 and one was previously in an investigator-sponsored study. Both patients had Trifunctional Protein (TFP) Deficiency type LC-FAOD, a type known to have a high mortality rate, and both had experienced severe disease manifestations when initiating UX007 treatment in the extension study.

In October 2019, we announced that the FDA accepted our NDA for UX007 for the treatment of LC-FAOD. The FDA assigned a PDUFA date of July 31, 2020. An Advisory Committee meeting is not expected at this time. The NDA filing is supported by a comprehensive package of data including results from a Company-sponsored Phase 2 study of UX007 in 29 patients, a long-term safety and efficacy extension study in 75 patients including 20 patients who were previously naïve to UX007, a retrospective medical record review of 20 original compassionate use patients, 67 patients treated through expanded access, and a randomized controlled investigator-sponsored study of 32 patients showing an effect on cardiac function. We have also submitted an application to regulatory authorities in Brazil, and we have initiated discussions with other regulatory authorities in the EU and the United Kingdom and Canada.

Please see "—License and Collaboration Agreements—Clinical Product Candidates—Baylor Research Institute" for a description of our license agreement with Baylor Research Institute.

DTX401 for the treatment of glycogen storage disease type Ia, or GSDIa

DTX401 is an adeno-associated virus 8, or AAV8, gene therapy clinical candidate for the treatment of patients with glycogen storage disease type Ia, or GSDIa, a disease that arises from a defect in G6Pase, an essential enzyme in glycogen and glucose metabolism. Hypoglycemia in patients with GSDIa can be life-threatening, and the accumulation of the complex sugar glycogen in certain organs and tissues can impair the ability of these tissues to function normally. If chronically untreated, patients can develop severe lactic acidosis, progress to renal failure, and potentially die in infancy or childhood. There are no approved pharmacologic therapies. GSDIa is the most common genetically inherited glycogen storage disease, with an estimated 6,000 patients in the developed world affected by GSDIa. DTX401 has been granted Orphan Drug Designation in both the United States and in the EU and the United Kingdom, Regenerative Medicine Advanced Therapy (RMAT) designation and Fast Track designation in the United States. In January 2019, we announced positive topline data from the first dose cohort (n=3, dose of 2.0 x 10^12 GC/kg) of the Phase 1/2 study of DTX401 in GSDIa. All three patients in Cohort 1 demonstrated clinically meaningful improvements in glucose control shown by time to hypoglycemia and reductions in cornstarch requirements.

In September 2019, we announced positive data from the second dose cohort (n=3, dose of 2.0 x 10^12 GC/kg) of the ongoing Phase 1/2 study of DTX401. All three patients in Cohort 2 showed a clinical response with improvements in glucose control and other metabolic parameters compared to baseline, and all three patients in Cohort 1 continued to demonstrate long-term, durable responses. All patients demonstrated increases in time to hypoglycemia compared to baseline during a controlled-fasting challenge, normalization of daily glucose levels which has allowed for clinically significant reductions in the amount of cornstarch, and meaningful improvements in assessments including lower lactate levels after treatment and early reductions in liver fat fraction. As of the data cutoff date of August 31, 2019, there have been no infusion-related adverse events and no treatment-related serious adverse events reported. All adverse events have been Grade 1 or 2. Four of the six patients in Cohorts 1 and 2 had mild, asymptomatic elevations in alanine aminotransferase (ALT), similar to what has been observed in other programs using AAV-based gene therapy, and were successfully treated with a reactive tapering course of steroids. Based on these results, we proceeded to a confirmatory expansion cohort of three additional patients at the second cohort dose of 6.0 × 10^12 GC/kg. All three patients have been dosed and data from the expansion cohort are expected in the first half of 2020. If the expansion cohort results are consistent with those observed to date, then the Phase 3 trial expected to begin in 2020 would study this dose level.

Please see "—License and Collaboration Agreements—Clinical Product Candidates—REGENXBIO Inc." for a description of our license agreement with REGENXBIO Inc.

DTX301 for the treatment of ornithine transcarbamylase, or OTC, deficiency

DTX301 is an AAV8 gene therapy product candidate designed for the treatment of patients with ornithine transcarbamylase, or OTC, deficiency. OTC is part of the urea cycle, an enzymatic pathway in the liver that converts excess nitrogen, in the form of ammonia, to urea for excretion. OTC deficiency is the most common urea cycle disorder and leads to increased levels of ammonia. Patients with OTC deficiency suffer from acute hyperammonemic episodes that can lead to hospitalization, adverse cognitive and neurological effects, and death. We estimate that there are approximately 10,000 patients in the developed world with OTC deficiency, of which we estimate approximately 80% are classified as late-onset, our target population. DTX301 has received Orphan Drug Designation in both the United States and in the EU and the United Kingdom and Fast Track Designation in the United States.

In January 2020, we announced data from the third dose cohort and longer-term data from the first two dose cohorts of the Phase 1/2 study of DTX301. The data demonstrated that up to six of the nine patients demonstrated a response as of the data cutoff date of December 9, 2019. In Cohort 3 (n=3, dose of 1.0 × 10^13 GC/kg), there were two confirmed female responders as well a third potential male responder who requires longer-term follow-up to confirm response status. In Cohort 2 (n=3, dose of 6.0 × 10^12 GC/kg), one female patient newly demonstrated a response starting at Week 52 which was confirmed at Week 78. Two previously disclosed responders in Cohort 1 (n=3, dose of 2.0 × 10^12 GC/kg) and Cohort 2 have remained clinically and metabolically stable at 104 and 78 weeks, respectively. As of the data cutoff date, there have been no infusion-related adverse events and no treatment-related serious adverse events reported in the study. All adverse events have been Grade 1 or 2. All three patients in Cohort 3 had mild, clinically asymptomatic elevations in ALT levels, similar to what has been observed in other programs using AAV-based gene therapy. All three patients have been responding to reactive tapering courses of steroids, and all patients remain clinically stable.

A fourth cohort is enrolling three patients at the 1.0 × 10^13 GC/kg dose, using prophylactic steroids. Patients will receive an 8-week tapering regimen of prophylactic steroids, starting at least 5 days prior to dosing with DTX301 at a starting steroid dose of 60 mg/day. The first patient is expected to be enrolled in the first half of 2020, and data from the prophylactic steroid cohort are expected in the second half of 2020.

We have also had discussions with the FDA regarding the potential Phase 3 study design. Ammonia is expected to be a primary endpoint based on direct FDA feedback to date, with ureagenesis as a measure of biologic activity that supports the decision for patients to discontinue alternate pathway medications.

Please see "—License and Collaboration Agreements—Clinical Product Candidates—REGENXBIO Inc." for a description of our license agreement with REGENXBIO Inc.

DTX201 for the treatment of Hemophilia A

DTX201 (BAY 2599023) is a Factor VIII gene therapy program for the treatment of hemophilia A that is partnered with Bayer Healthcare LLC, or Bayer, utilizing our proprietary HeLa platform. Hemophilia A is the most common form of hemophilia with approximately 144,000 patients in the developed world. Data from the first dose cohort (n=2, dose of 5.0 x 10^12 GC/kg) of the Phase 1/2 study of DTX201 in hemophilia A was presented at the American Society of Hematology Annual Meeting in December 2019, and longer-term data from the first dose cohort and new data from the second dose cohort (n=2, dose of 1.0 x 10^13 GC/kg), was presented at the European Association for Haemophilia and Allied Disorders conference in February 2020. One patient in Cohort 1 and both patients in Cohort 2 demonstrated clinically meaningful improvements in FVIII levels. The patient in Cohort 1 experienced four bleeds post-treatment compared to 99 bleeds the prior year. Both patients in dose cohort 2 achieved clinically meaningful FVIII levels out to 24 and 30 weeks. Patient 4 in Cohort 2 has been bleed-free and treatment-free for up to seven months, as of the data cutoff. Patient 4 had mild ALT/AST elevations that were managed with a short tapering course of corticosteroids. Dose escalation in the Phase 1/2 study is ongoing.

Please see "—License and Collaboration Agreements—Clinical Product Candidates—Bayer" for a description of our license agreement with Bayer.

GTX-102 for the treatment of Angelman Syndrome

GTX-102, is an antisense oligonucleotide, or ASO, that is being developed for the treatment of Angelman syndrome, a debilitating and rare neurogenetic disorder, in collaboration with GeneTx Biotherapeutics LLC, or GeneTx.

In September 2019, we announced that the FDA granted Orphan Drug Designation and Rare Pediatric Disease Designation to GTX-102 for the treatment of Angelman syndrome.

In January 2020, we announced that GeneTx's IND Application for GTX-102 was filed with the FDA and is now active. Enrollment in the Phase 1/2 study is expected to begin in the first half of 2020.

Please see "—License and Collaboration Agreements—Clinical Product Candidates—GeneTx" for a description of our collaboration agreement with GeneTx.

Preclinical Pipeline

UX701 for the treatment of Wilson Disease

UX701 is in preclinical development for Wilson disease, a rare inherited disorder caused by mutations in the ATP7B gene, which results in deficient production of ATP7B, a protein that transports copper. Loss of function of this copper-binding protein results in the accumulation of copper in the liver and other tissues, most notably the central nervous system. Patients with Wilson disease experience hepatic, neurologic and/or psychiatric problems. Those with liver disease can experience such symptoms as fatigue, lack of appetite, abdominal pain and jaundice, and can progress to fibrosis, cirrhosis, life-threatening liver failure and death. Wilson disease can be treated by reducing copper absorption or removing excess copper from the body using life-long chelation therapy, but unmet needs exist because some treated patients experience clinical deterioration and severe side effects. Wilson disease affects more than 50,000 individuals in the developed world. An IND for UX701 is expected by the end of 2020.

UX053 for the treatment of glycogen storage disease type III, or GSDIII

Our preclinical candidate UX053 is being developed for the treatment of GSDIII, a disease caused by a glycogen debranching enzyme (AGL) deficiency that results in glycogen accumulation in the liver and muscle. GSDIII can cause hepatomegaly, hypoglycemia, hyperlipidemia, some progressive liver cirrhosis, and muscle disease later in life, and affects more than 10,000 patients in the developed world.

Please see "—License and Collaboration Agreements—Preclinical Pipeline—Arcturus" for a description of our collaboration agreement with Arcturus.

UX068 for the treatment of creatine transporter deficiency, or CTD

UX068 is in preclinical development for the treatment of CTD, an X-linked recessive disorder due to mutations in the SLC6A8 gene. Patients with CTD can suffer from CNS deficits, seizures, progressive intellectual disability, autism, speech/language/gross motor delays, and muscle hypotonia and hypotrophy. CTD affects an estimated 30,000 to 50,000 patients in the developed world.

Other preclinical programs

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

Competition

In the case of indications that we are targeting, it is possible that other companies may produce, develop, and commercialize compounds that might treat these diseases.

With respect to Crysvita, 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 Crysvita, if approved, in some countries.

With respect to Mepsevii, we are not aware of any other compounds currently in clinical development for MPS VII, but it is possible that other companies may produce, develop, and commercialize compounds that might treat this disease. 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 VII 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. LC-FAOD is commonly treated with diet therapy and MCT oil. UX007 may compete with this approach. 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. Investigators are testing triheptanoin in clinical studies across multiple indications, including LC-FAOD. 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. Other companies may also utilize other approaches, such as gene therapy, to treat LC-FAOD. In addition, Reneo Pharmaceuticals is developing REN001, a PPAR delta agonist, in Phase 1b for LC-FAOD and other genetic myopathies.

With respect to DTX301, the current treatments for patients with OTC deficiency are nitrogen scavenging drugs and severe limitations in dietary protein. Drug therapy includes sodium phenylbutyrate (Buphenyl) and glycerol phenylbutyrate (Ravicti), both nitrogen scavengers that help eliminate excess nitrogen, in the form of ammonia, by facilitating its excretion. A novel formulation of sodium phenylbutyrate, ACER-001, is in Phase 2 clinical testing by Acer Therapeutics. During a metabolic crisis, patients routinely receive carbohydrate and lipid rich nutrition, including overnight feeding through a nasogastric tube, to limit bodily protein breakdown and ammonia production. In acute cases, ammonia must be removed by dialysis or hemofiltration. Liver transplant may also be a solution for OTC deficiency. In addition, Kaleido Biosciences is developing KB195, a synthetic glycan, in Phase 2 for urea cycle disorders, including OTC deficiency.

With respect to DTX401, there are currently no pharmacologic treatments for patients with GSDIa and we are not aware of any programs in clinical development.

With respect to GTX-102, there are currently no approved drugs for Angelman syndrome. Many patients take general treatments to try to manage specific symptoms, such as seizures or sleep disturbances, but there are no treatments available that address the underlying biology of the disease. We are aware of other ASOs in preclinical development for Angelman syndrome, as well as gene therapy programs. In addition, Ovid Therapeutics is developing OV101, a $GABA_A$ receptor agonist, in Phase 3 for Angelman syndrome.

License and Collaboration Agreements

Our products and current product candidate pipeline have been either in-licensed from academic institutions or derived from partnerships with other pharmaceutical companies. Following is a description of our significant license and collaboration agreements.

Approved Products

Kyowa Kirin Co., Ltd.

In August 2013, we entered into a collaboration and license agreement with KKC. Under the terms of this collaboration and license agreement, as amended, we and KKC currently collaborate on the development and commercialization of Crysvita in the field of orphan diseases in the United States and Canada, or the "profit-share territory", and in the EU, United Kingdom, and Switzerland, or the European territory, and we 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 KKC, we are the lead party for development activities in the profit-share territory and in the European territory until the applicable transition date; we are also the lead party for core development activities conducted in Japan and Korea for which the core development plan is limited to clinical trials mutually agreed to by us and KKC. We 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 KKC and KKC is responsible for 100% of the costs for development activities in Japan and Korea. In April 2023, which is the transition date for the profit-share territory, and following the applicable transition date for the European territory, KKC 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 KKC. Crysvita was approved in the EU in February 2018 and was approved by the FDA in April 2018. As described below, we and KKC share commercial responsibilities and profits in the profit-share territory until April 2023, KKC has the commercial responsibility in the European territory, and we are responsible for commercializing burosumab in Latin America.

In the profit-share territory, KKC books sales of products and we have the sole right to promote the products for a specified period of time, with KKC increasingly participating in the promotion of the products until April 2023, which is five years from commercial launch, after which KKC will have the right to promote the products, subject to a limited promotion right retained by us. See "Item I.A. Risk Factors" for additional information on the risks related to the expiration of our exclusive right to promote Crysvita in the profit-share territory. In the European territory, KKC books sales of products and has the sole right to promote and sell the products. In Latin America, we book sales of products and have the sole right to promote and sell the products.

KKC manufactures and supplies all quantities of product for clinical studies. KKC also supplies all quantities of product for commercial sales in the profit-share territory and in Latin America. The supply price in the profit-share territory and Latin America is 35% of net sales price through December 31, 2022 and 30% thereafter.

The remaining profit or loss from commercializing products in the profit-share territory is shared between us and KKC on a 50/50 basis until April 2023. 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. KKC is also required to pay a royalty of up to 10% based on net sales in the European territory. We sold our interest in the European territory royalty to Royalty Pharma in December 2019. In Latin America, we pay to KKC a low single-digit royalty on net sales. Our and KKC's obligations to pay royalties will continue on a country-by-country basis for so long as we or KKC, as applicable, are selling products in such country.

In May 2017, we signed an agreement with a wholly-owned subsidiary of KKC pursuant to which we were granted the right to commercialize Crysvita in Turkey. KKC's subsidiary has the option to assume responsibility for commercialization efforts from us, after a certain minimum period.

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, Turkey, or Latin America, unless the agreement is terminated in accordance with its terms.

KKC may terminate the agreement in certain countries or territories based upon our failure to meet certain milestones. Specifically, if we do not make a first commercial sale, on a country-by-country basis, in Latin America by certain deadlines, KKC 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 KKC 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 KKC, unless such termination is the result of KKC'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 KKC 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 Crysvita under the agreement and our obligations to share development costs will cease, and the program will revert to KKC, 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 Mepsevii. 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 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, upon reaching a certain level of 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 Europe, until the later expiration of any orphan drug exclusivity. 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.

Clinical Product Candidates

Baylor Research Institute

In September 2012, we entered into a license agreement with Baylor Research Institute, or BRI, under which we exclusively licensed certain intellectual property related to triheptanoin. 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 LC-FAOD. The license grant includes the sole right to develop, manufacture, and commercialize licensed products for all human and animal uses. 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 LC-FAOD or an orphan disease covered by our license from BRI. We may make future payments of up to $5.3 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 by its terms, 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.

REGENXBIO Inc.

In October 2013, we entered into an exclusive license agreement with REGENXBIO Inc., or REGENX, under which we were granted an option to develop products to treat hemophilia A, OTC deficiency and GSDIa. Under the 2013 license agreement, REGENX granted us an exclusive worldwide license to make, have made, use, import, sell, and offer for sale licensed products with respect to such disease indications, subject to certain exclusions. We do not have the right to control prosecution of the in-licensed patent applications, and our rights to enforce the in-licensed patents are subject to certain limitations. Under the 2013 license agreement, we pay or will pay REGENX an annual maintenance fee and certain milestone fees per disease indication, low to mid single-digit royalty percentages on net sales of licensed products, and milestone and sublicense fees, if any, owed by REGENX to its licensors as a result of our activities under the 2013 license agreement. We are required to develop licensed products in accordance with certain milestones. In the event that we fail to meet a particular milestone within established deadlines, we can extend the relevant deadline by providing a separate payment to REGENX. The 2013 license agreement will expire upon the expiration, lapse, abandonment, or invalidation of the last claim of the licensed intellectual property to expire, lapse, or become abandoned or unenforceable in all the countries of the world. Upon expiration, our know-how license will become non-exclusive, perpetual, irrevocable and royalty-free with respect to licensed know-how that REGENX owns in the field and will continue with respect to all of REGENX's other know-how in the field under certain of its licenses for so long as its rights from those licensors continue. Subject to certain obligations to Bayer, we may terminate the 2013 license agreement upon prior written notice or for a material breach. REGENX may terminate the license agreement if we or our controlling affiliate become insolvent, are late in paying money due, commence certain actions relating to the licensed patents or materially breach the agreement. If the 2013 license agreement is terminated with respect to an indication, we grant certain rights to REGENX, including transferring ownership of any applicable regulatory approvals and granting an exclusive license under certain of our intellectual property for use with respect to products covered by the intellectual property we had licensed from REGENX in that indication.

In March 2015, we entered into an option and license agreement with REGENX under which we were granted an option to develop product candidates to treat Wilson disease and another disease indication. We have exercised our options available to develop a product candidate under this agreement. The 2015 option and license agreement grants us an exclusive worldwide license to make, have made, use, import, sell, and offer for sale licensed products with respect to such disease indications, subject to certain exclusions. We do not have the right to control prosecution of the in-licensed patent applications, and our rights to enforce the in-licensed patents are subject to certain limitations. Under the 2015 option and license agreement, we pay or will pay REGENX an annual maintenance fee and certain milestone fees per disease indication, mid to high single-digit royalty percentages on net sales of licensed products, and mid-single to low double-digit percentages of any sublicense fees we receive from sublicenses for the licensed intellectual property rights. We are required to develop licensed products in accordance with certain milestones. In the event that we fail to meet a particular milestone within established deadlines, we can extend the relevant deadline by providing a separate payment to REGENX. The 2015 option and license agreement will expire upon the expiration of the royalty obligations with respect to all licensed products for all licensed indications under all licenses granted under all exercised commercial options. Upon expiration, our know-how license will become non-exclusive, perpetual, irrevocable and royalty-free with respect to licensed know-how that REGENX owns in the field and will continue with respect to all of REGENX's other know-how in the field under certain of its licenses for so long as its rights from those licensors continue. We may terminate the 2015 option and license agreement upon prior written notice or for a material breach. REGENX may terminate the 2015 option and license agreement if we or our controlling affiliate become insolvent, are late in paying money due, commence certain actions relating to the licensed patents or materially breach the agreement. If the 2015 option and license agreement is terminated with respect to an indication, we grant certain rights to REGENX, including transferring ownership of any applicable regulatory approvals and granting an exclusive license under certain of our intellectual property for use with respect to products covered by the intellectual property we had licensed from REGENX in that indication.

Bayer

In June 2014, we entered into an agreement with Bayer to research, develop and commercialize AAV gene therapy products for treatment of hemophilia A, which was amended and restated in June 2019. Under this agreement, we granted Bayer an exclusive license to develop and commercialize one or more novel gene therapies for hemophilia A. We are responsible for the development of DTX201 through a proof-of-concept clinical trial, with reimbursement from Bayer for project costs. Bayer is responsible operationally, including for conducting the proof-of-concept clinical trial, and will incur the costs of the conduct of the trial. Upon the successful demonstration of clinical proof of concept, Bayer agreed to use commercially reasonable efforts to manage and fund any subsequent clinical trials and commercialization of gene therapy products for treatment of hemophilia A. Bayer will have worldwide rights to commercialize the potential future product.

Under the agreement, Bayer paid us an upfront cash payment and will pay us development and commercialization milestone payments, and tiered royalties based on product sales. The agreement expires on a licensed treatment-by-licensed treatment and country-by-country basis until the later of ten years from the date of first commercial sale or when patent claims have expired, lapsed, been abandoned, or been invalidated in such country. Either party may terminate the agreement for an uncured material breach by the other party. Bayer may terminate the agreement upon prior notice to us, either in its entirety or with respect to certain territories subject to the agreement. Bayer may also terminate the agreement upon notice of a product's failure to meet certain criteria or after the successful completion of certain Phase 1 trials in the event Bayer makes a good faith determination that there is a material safety issue with respect to such product. Either party may terminate the agreement upon bankruptcy or insolvency of the other party, and we may terminate the agreement if Bayer institutes certain actions. Under certain termination circumstances, we would have worldwide rights to the terminated program(s).

University of Pennsylvania

In January 2015, we entered into an agreement with the University of Pennsylvania to sponsor certain research of Dr. Wilson at University of Pennsylvania School of Medicine related to liver gene therapy and hemophilia. Under the agreement, the University of Pennsylvania granted us an option to obtain a worldwide, non-exclusive or exclusive, royalty-bearing license, with the right to sublicense, under certain patent rights conceived, created or reduced to practice in the conduct of the research. We are required to reimburse the University of Pennsylvania for filing, prosecuting and maintaining such patent rights unless and until we decline to exercise our option. The University is required to provide us with task-based, scientific reports of progress and results of the research, and granted us a royalty-free, nontransferable, non-exclusive right to copy and distribute any research reports furnished to us for any reasonable purpose, provided the results are not made publicly available until certain conditions are met, and the right to use, disclose and otherwise exploit the research results for any reasonable purpose, subject to similar restrictions on our public disclosure of the research results.

This agreement expires on the earlier of the completion of certain tasks and activities or December 31, 2021. The agreement may be extended further, or renewed, by mutual agreement. If extended or renewed, then either party may terminate the agreement if Dr. Wilson becomes unavailable and an acceptable substitute is not found within a certain period of time, or if we fail to mutually agree on an acceptable work plan and budget for the sponsored research. We may also terminate the sponsored research agreement upon written notice, as long as we have met all of our payment and performance obligations. Either party may terminate this agreement for an uncured material breach. In the event of termination, we shall pay University of Pennsylvania the amount needed to cover costs through the effective termination date as well as allowable commitments extending beyond the termination date (up to one-fourth of the total budget).

In May 2016, we entered into a research, collaboration and license agreement with the University of Pennsylvania under which we are collaborating on the pre-clinical development of gene therapy products for the treatment of citrullinemia type I, phenylketonuria, and Wilson disease, each, a Subfield. Under the agreement, we were granted an exclusive, worldwide, royalty-bearing right and license to certain patent rights arising out of the research program, and a non-exclusive, worldwide, royalty-bearing right and license to certain University of Pennsylvania intellectual property, in each case to research, develop, make, have made, use, sell, offer for sale, commercialize and import licensed products in each Subfield for the term of the agreement. We will fund the cost of the research program and will be responsible for clinical development, manufacturing and commercialization of each Subfield. In addition, we will be required to make milestone payments (up to a maximum of $5 million per Subfield) if certain development milestones are achieved over time, and to pay low to mid single-digit royalties on net sales of each Subfield's licensed products. We will also make milestone payments of up to $25.0 million per approved product if certain commercial milestones are achieved.

GeneTx

In August 2019, we announced an agreement with GeneTx to collaborate on the development of GeneTx's GTX-102. Under the terms of the agreement, we made an upfront payment of $20.0 million which included an exclusive option to acquire GeneTx. This option may be exercised any time prior to 30 days following notice of FDA acceptance of the IND for GTX-102. In February 2020, we paid $25.0 million following acceptance of the IND to maintain the option to acquire GeneTx until the earlier of 30 months from the first dosing of a patient in a planned Phase 1/2 study (subject to extensions) or 90 days after results are available from that study. If we exercise the purchase option, we will pay a purchase price to acquire GeneTx, payments upon achieving regulatory and commercial milestones, and royalties on any product sales.

Preclinical Pipeline

Arcturus

We signed a research collaboration and license agreement with Arcturus 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.

In June 2019, we announced the expansion of our research and collaboration arrangement with Arcturus Therapeutics Holdings Inc., or Arcturus, to discover and develop mRNA, DNA and siRNA therapeutics for up to 12 rare disease targets pursuant to the terms of an amendment to the Research Collaboration and License Agreement, or License Agreement, and Equity Purchase Agreement. In connection with the amendment to the License Agreement, we made a $6.0 million cash upfront payment to Arcturus and also purchased 2,400,000 shares of Arcturus' common stock at a stated value of $10.00 per share. We have an option to purchase an additional 600,000 shares of Arcturus' common stock at $16.00 per share. Arcturus is entitled to preclinical, clinical, regulatory, and sales milestone payments for each product developed under the collaboration. Under the amended license agreement, certain early-stage milestone payments are reduced and the total potential milestone payments are increased due to the expanded number of targets. Arcturus is also entitled to reimbursement of related research expenses and royalties on commercial sales.

Patents and Proprietary Rights

The proprietary nature of, and protection for, our products, 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 products, 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 products, 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 use other means to protect our proprietary rights, including the pursuit of 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 "Government Regulation—U.S. Government Regulation — Orphan Designation and Exclusivity," "Government Regulation—U.S. Government Regulation — Pediatric Studies and Exclusivity," "Government Regulation—U.S. Government Regulation — Patent Term Restoration," "Government Regulation—U.S. Government Regulation — Biosimilars and Exclusivity," "Government Regulation—U.S. Government Regulation — Abbreviated New Drug Applications for Generic Drugs and New Chemical Entity Exclusivity," and "Government Regulation—EU 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 product candidates 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 product candidates, 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 by 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."

We own or in-license a number of patents in the U.S. and foreign countries that cover our products, product candidates, and methods of their use. With respect to our owned or in-licensed issued patents in the U.S. and Europe, we may be entitled to obtain an extension of patent term to extend the patent expiration date. For example, in the U.S., this extended coverage period is known as patent term extension (PTE) and can only be obtained provided we apply for and receive a marketing authorization for a product. The period of extension may be up to five years beyond the expiration of the patent, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended. In Europe, Supplementary Protection Certificates (SPC) may also be available to patents, which would be available by applying to the member states. However, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. 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 exclusivity positions for our commercial products, Mepsevii and Crysvita, and our clinical-stage product candidates as of December 31, 2019 are summarized below.

Crysvita (Burosumab) Exclusivity

We have in-licensed rights from KKC to patents and patent applications relating to Crysvita and its use for the treatment of XLH and various other hypophosphatemic conditions. Pursuant to this license, we have rights to a number of issued patents and pending applications, including five issued U.S. patents, 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 the issued patents in the U.S. are from 2022 to 2029 (without extension of patent term), while the issued patents outside the U.S. expire between 2021 and 2028 (without extension of patent term). KKC has applied for an extension of patent term in the U.S. and Europe for Crysvita to 2032 and 2033, respectively. We also jointly own with KKC a pending application in the U.S. and corresponding foreign patent applications relating to dosing regimens for administration of anti-FGF23 antibodies, including Crysvita. Any patents issuing from these jointly-owned applications would be expected to expire in 2035. In addition to the foregoing patent protections, Crysvita is protected in the U.S. by regulatory data exclusivity until 2030 and by orphan drug exclusivity for treating XLH until 2025.

Mepsevii (Vestronidase Alfa) Exclusivity

We own four issued U.S. patents covering Mepsevii and its use in the treatment of lysosomal storage disorders such as MPS VII. The patents in the U.S. expire in 2035. Mepsevii is also protected in the U.S. by regulatory data exclusivity until 2029 and by orphan drug exclusivity for treating MPS VII until 2024. Outside the U.S., we own issued patents expiring in 2035 in Australia, China, Colombia, Europe, Japan, Mexico, Russia, and Singapore, as well as pending patent applications in other territories, which cover Mepsevii and its use in the treatment of MPS VII.

UX007 Exclusivity

We have an exclusive license from the Baylor Research Institute, or BRI, to patents and patent applications relating to the UX007 composition and its use for the treatment of FAOD. In the U.S., the in-licensed BRI patent portfolio includes issued patents with claims covering the UX007 composition that expire between 2020 and 2025 (without extension of patent term). The BRI portfolio additionally includes issued U.S. and foreign patents with claims covering the use of UX007 for the treatment of FAOD that expire in 2020 (without extension of patent term). We also own a pending U.S. patent application and corresponding foreign patent applications relating to our pharmaceutical-grade UX007 composition. Any patents issuing from these owned applications would be expected to expire in 2034. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries. UX007 has received orphan designation in the U.S. for FAOD and in Europe for various subtypes of FAOD.

DTX301 Exclusivity

We have in-licensed patents and patent applications owned by the University of Pennsylvania, or UPENN, relating to various adeno-associated viruses and vectors utilizing the capsids of those viruses. These patents and patent applications are licensed or sublicensed to REGENXBIO and sublicensed to us. Our product candidate DTX301 utilizes an AAV8 capsid and a codon-optimized version of the OTC gene. The in-licensed patents relevant to the AAV8 capsid expire between 2022 and 2024 in the U.S., and in 2022 in foreign countries. Our in-license also includes an issued U.S. patent expiring in 2035 (without extension of patent term) and corresponding foreign patent applications covering the codon-optimized version of the OTC gene used in DTX301. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries. DTX301 for the treatment of OTC deficiency has received orphan drug designation in the U.S. and Europe.

DTX401 Exclusivity

We have two in-licenses to patents and patent applications covering elements of our DTX401 product candidate. First, we have in-licensed patents owned by UPENN and sublicensed to us by REGENXBIO relating to the AAV8 capsid used in DTX401 that expire between 2022 and 2024 in the U.S., and in 2022 in foreign countries. Second, we have a non-exclusive license from the National Institutes of Health (NIH) to issued U.S. and European patents expiring in 2034 (without extension of patent term) and corresponding patent applications in other territories covering a recombinant nucleic acid construct used in DTX401 that includes a codon-optimized version of the G6Pase gene. We intend to pursue marketing and orphan drug exclusivity periods that are available under regulatory provisions in certain countries. DTX401 for the treatment of GSD1a has received orphan drug designation in the U.S. and Europe.

Trademarks

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

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 products and product candidates for use in preclinical, clinical, and commercial applications. We do not own or operate manufacturing facilities for the cGMP production of clinical or commercial quantities of our product candidates. We do, however, have process and analytical development and QC lab capabilities focused on the gene therapy technologies. The use of contracted manufacturing and reliance on collaboration partners is relatively cost-efficient and has minimized 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. All of our third-party manufacturers are subject to periodic audits to confirm compliance with applicable regulations and must pass inspection before we can manufacture our drugs for commercial sales.

While our third-party manufacturers have met our current manufacturing requirements, we intend to build our own GMP gene therapy manufacturing plant to mitigate potential program timeline delays, control manufacturing costs and reduce manufacturing lead times. The recent addition of GMP QC lab capabilities is an example of this strategy. For the other non-gene therapy modalities, we primarily use third-party manufacturers 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.

Products

Mepsevii

The Mepsevii drug substance and drug product are manufactured by Rentschler Biopharma SE, or Rentschler, under non-exclusive commercial supply and services agreements effective December 2017 and January 2018, respectively. The drug substance agreement has an initial term of five years, which will be automatically extended for another five years following the initial term, and will continue in full force and effect for its term unless earlier terminated. Following the initial term, we and Rentschler can withdraw from the agreement without cause upon prior notice for specified periods. In addition, either party may terminate the agreement if the other party breaches a material provision of the agreement and such breach remains uncured for a specified period following receipt by the breaching party of written notice of such breach. The drug product agreement expires on December 31, 2025 and will continue in full force and effect for its term unless earlier terminated. Either party may terminate the agreements with immediate effect if the other party violates or breaches certain obligations set forth in the agreement, undergoes a material change in control, or infringes its intellectual property rights. We can also terminate the agreements if Rentschler loses the right to operate under the agreement. Either party can also terminate the agreements if Rentschler is unable to deliver its agreed upon services for a certain period in the case of a force majeure event. The cell line to produce Mepsevii is specific for this product and is in our control and stored in multiple secure locations. All other raw materials are commercially available. We intend to transfer the fill and finish activities for the manufacture of Mepsevii to a new site as the Rentschler manufacturing site in Laupheim, Germany is being discontinued. In preparation of this activity, we intend to maintain sufficient inventory levels as we identify an alternative supplier and transfer the fill and finish activities for Mepsevii to such supplier. See “Item IA. Risk Factors” for additional information on the risks associated with the transfer of the Mepsevii finish and fill activities to an alternative supplier.

Crysvita

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

Product Candidates

UX007

The pharmaceutical-grade drug substance for UX007 is manufactured by IOI Oleo GmbH, or IOI Oleo, in Germany under an exclusive worldwide supply agreement, subject to certain limitations, executed in 2012 with an initial term of three years. The agreement automatically renews for two-year periods at the end of each then current term 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. Multiple parties have manufactured the UX007 drug product for us, which is not considered a very specialized task.

DTX301

The drug substance and drug product for DTX301, our AAV product candidate, are manufactured on a non-exclusive basis by a contract manufacturing organization, or CMO, pursuant to cGMP requirements.

DTX301 is currently manufactured using HEK293 adherent mammalian cells. Adherent and suspension HEK293 cells are straightforward to grow and transfect readily, and as a result, are widely used in the biotechnology industry to produce therapeutic proteins and viral vectors for gene therapy on a small scale. Vectors produced using HEK293 cells have been, or are being, used safely in multiple clinical trials, including trials conducted in the United States and EU by other biopharmaceutical companies and academic government institutions. A key advantage of the HEK293 cell manufacturing system is flexibility and the relative speed with which AAV vectors can be manufactured for early Phase 1/2 clinical trials, allowing the establishment of early indications of therapeutic benefit in patients. As we advance and scale up our processes for Phase 3 clinical and commercial scale manufacturing, we intend to transition from the HEK293 cell manufacturing scale used for our DTX301 Phase 1/2 programs to a cell-based suspension bioreactor format.

DTX401

Similar to DTX301, the drug substance and drug product for DTX401 are manufactured on a non-exclusive basis by a CMO pursuant to cGMP requirements.

DTX401 is currently manufactured using HEK293 suspension mammalian cells. Similar to DTX301, HEK293 cells are widely used in the biotechnology industry and the regulatory agencies in the United States and EU are familiar with the technology. As the clinical program advances we may consider alternate cell manufacturing systems such as HeLa cell systems.

Commercialization and Product Support

We have built our own commercial organizations in North America, Europe and Latin America to effectively support the commercialization of our products and product candidates, if approved, and we expect to expand on these efforts. Our intention is to expand our product portfolio and its geographic scope, whether via acquisition, strategic partnerships, or through the continued development of our proprietary pipeline. We may elect to utilize strategic partners, distributors, or contract management organizations to assist in the commercialization of our products. The commercial infrastructure for rare disease products typically consists of a targeted, specialty field organization that educates a limited and focused group of physicians supported by field management and internal support teams, which includes our patient support services hub and distribution team. 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 focuses on 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 stakeholders such as managed care organizations, group-purchasing organizations, specialty pharmacies, and government accounts. To develop the appropriate commercial infrastructure, we will have to invest a significant amount of financial and management resources, some of which will be committed prior to regulatory approval of the products that they are intended to support.

We continue to build a medical affairs organization and multiple capabilities across North America, Europe, Turkey, and Latin America to meet the scientific educational needs of the healthcare providers and patients in the rare disease community, focusing on providing accurate disease state and balanced product information across our portfolio for appropriate management of patients with rare disorders.

Medical affairs is comprised of the following capabilities in support of our mission: medical information, patient advocacy, patient diagnosis, medical science liaisons, research and educational grants. Medical affairs will engage as early as Phase 1 and will continue work throughout the lifecycle of each product and product candidate as dictated by the specific scientific needs in each therapeutic area.

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. We must obtain the requisite approvals from regulatory authorities in the United States and foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Accordingly, our operations are and will be subject to a variety of regulations and other requirements, which vary from country to country. 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.

Global Regulation of Clinical Studies

Clinical studies involve the administration of an investigational medicinal product to human subjects under the supervision of qualified investigators in accordance with protocols, Good Clinical Practices, or GCP, the ethical principles that have their origin in the Declaration of Helsinki and applicable regulatory requirements. A protocol for each clinical study and any subsequent protocol amendments are typically submitted to the FDA or other applicable regulatory authorities as part of an IND or clinical trial application, or CTA. Additionally, approval must also be obtained from each clinical study site's institutional review board, or IRB, or Ethics Committee, or EC, before the studies may be initiated, and the IRB or EC 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. Regulatory authorities may condition approval of a marketing application 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.

A pivotal study is a clinical study that adequately meets regulatory authority 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 regulatory authorities 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.

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 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.

The process required by the FDA before product candidates may be marketed or sold 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;
- conducting adequate and well-controlled human clinical studies to establish the safety and efficacy of the product candidate for each proposed indication under an active IND and approved by an independent IRB representing each clinical site;
- preparation of and submission to the FDA of a new drug application, or 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 inspection of one or more clinical sites to assure compliance with GCP; and
- FDA review and approval of an NDA or BLA.

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 a significant application user fee, unless waived.

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. 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.

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. 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, 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.

Furthermore, the FDA has made available expedited programs to sponsors of regenerative medicine therapies that have been granted designation as a regenerative medicine advanced therapy (RMAT). Regenerative medicine therapies include cell therapies, therapeutic tissue engineering products and human cell and tissue products. A sponsor may seek RMAT designation if its regenerative medicine product is intended for a serious condition and preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such condition.

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. 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.

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 2 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.

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.

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 and New Chemical Entity Exclusivity

The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, authorized the FDA to approve generic drugs that are bioequivalent (i.e. identical) to previously approved branded drugs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the FDA. 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 bioequivalent 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.

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.

When an ANDA applicant files its application with the FDA, it must certify, among other things, that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable, which 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.

Patent Term Restoration

Some of our U.S. patents may be eligible for limited patent term extension under 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. Thus, for each approved product, we may apply for restoration of patent term for one of our related owned or licensed patents to add patent life beyond the original expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant NDA or BLA.

EU Regulation

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

Authorization Procedures

Medicines can be authorized by using the centralized authorization procedure or national authorization procedures. The centralized authorization procedure results in a single marketing authorization issued by the European Medicines Agency, or EMA, that is valid across the European Economic Area, or EEA, which is comprised of the 27 member states of the EU plus Norway, Iceland, and Lichtenstein. 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. Medicines that fall outside the mandatory scope of the centralized procedure have three routes to authorization: (i) they can be authorized under the centralized procedure if they concern a significant therapeutic, scientific or technical innovation, or if their authorization would be in the interest of public health; (ii) they can be authorized under a decentralized procedure where an applicant applies for simultaneous authorization in more than one EU country; or (iii) they can be authorized in a EU member state in accordance with that state's national procedures and then be authorized in other EU countries by a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization (mutual recognition procedure).

A Pediatric Investigation Plan, or PIP, and/or a request for waiver or deferral, is required for submission prior to submitting an MAA. A PIP describes, among other things, proposed pediatric studies and their timing relative to clinical studies in adults and an MAA must comply with the PIP to be validated.

MAA Review and Approval Timeframe and Accelerated Assessment

Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA that has been validated is 210 days, excluding time taken by an applicant to respond to questions. A favorable opinion on the application by the Committee for Medicinal Products for Human Use, or CHMP, will typically result in the granting of the marketing authorization within 67 days of receipt of the opinion. Generally, the entire review process takes approximately one year. 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 time taken by an applicant to respond to questions.

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.

PRIME Program

PRIME is a program launched by the EMA to enhance support for the development of medicines that target an unmet medical need. The program focuses on medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options. These medicines are considered priority medicines by EMA. To be accepted for PRIME, a medicine has to show its potential to benefit patients with unmet medical needs based on early clinical data. Through PRIME, the EMA offers early and proactive support to medicine developers to optimize development plans and the generation of robust data on a medicine's benefits and risks and enables accelerated assessment of medicines applications.

Orphan Designation and Exclusivity

As in the United States, we may apply for designation of a product as an orphan drug for the treatment of a specific indication in the EU before the application for marketing authorization is made. 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. 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 does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

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 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.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to regulatory approvals are subject to pervasive and continuing regulation by the regulatory authorities, including, among other things, requirements relating to formal commitments for post approval clinical trials and studies, manufacturing, recordkeeping, periodic reporting, product sampling and distribution, marketing, labeling, 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 regulatory authority review and approval.

Drug manufacturers are subject to periodic unannounced inspections by regulatory authorities and country or 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 regulatory approval before being implemented. 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.

Pharmaceutical Coverage, Pricing and Reimbursement

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.

In the EU, 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 patients. 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. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

Other Healthcare Laws and Compliance Requirements

We are subject to various laws targeting, among other things, fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing, and education programs. 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, as amended, which prohibits executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters and imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- the EU General Data Protection Regulation (GDPR), which seeks to harmonize data privacy laws across Europe to ensure data subjects' fundamental right to privacy in the EU in the digital age by imposing requirements and limitations relating to the processing, storage, purpose of collection, accuracy, security and transmission of personal data and the notification of regulation authorities about data breaches, accompanied by a strong sanctioning mechanism;
- the 21st Century Cures Act, or the Cures Act, which introduced a wide range of reforms, such as broadening the types of data required to support drug approval, extending protections for generic competition, accelerating approval of breakthrough therapies, expanding the orphan drug product program, requiring disclosures about compassionate care programs, and clarifying how manufacturers communicate about their products;
- 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; and
- state and foreign law equivalents of each of the above federal laws, such as transparency laws, anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and privacy and security of health information laws.

Additional Regulation

The U.S. Foreign Corrupt Practices Act or FCPA, to which we are subject, prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. Similar laws exist in other countries, such as the United Kingdom, that restrict improper payments to public and private parties. Many countries have laws prohibiting these types of payments within the respective country. In addition to these anti-corruption laws, we are subject to import and export control laws, tariffs, trade barriers, economic sanctions and regulatory limitations on our ability to operate in certain foreign markets.

In addition, federal, state and foreign government bodies and agencies have adopted, are considering adopting, or may adopt laws and regulations regarding the collection, use, storage and disclosure of personally identifiable information or other information treated as confidential obtained from consumers and individuals.

We are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other present and potential federal, state or local regulations. These and other laws govern our use, handling and disposal of various biological and chemical substances used in, and waste generated by, our operations.

Customers

Our customers include collaboration partners, drug wholesalers, and retail pharmacy distributors. For the year ended December 31, 2019, 80% of our total revenues were generated under our collaboration agreement with KKC.

Employees

As of December 31, 2019, we had 740 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.

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*. Our Internet website address is *www.ultragenyx.com.* No portion of our website is incorporated by reference into this Annual Report.

You are advised to read this Annual Report 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. The SEC maintains information for electronic filers (including Ultragenyx) at its website at *www.sec.gov*. 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 Annual Report, including our financial statements and notes thereto, before deciding to invest in our common stock. If any of the following risks actually materialize, 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 have a history of operating losses and anticipate that we will continue to incur losses for the foreseeable future.

We are a biopharmaceutical company with a history of operating losses, and anticipate continuing to incur operating losses for the foreseeable future. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have devoted substantially all of our financial resources to identifying, acquiring, and developing our products and product candidates, including conducting clinical studies, developing manufacturing processes, manufacturing product candidates for clinical studies, and providing selling, general and administrative support for these operations. The amount of our future net losses will depend, in part, on non-recurring events, the success of our commercialization efforts, and the rate of our future expenditures. 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 products and product candidates;
- change or add additional manufacturers or suppliers;
- seek to expand upon or build our own manufacturing-related facilities and capabilities, including our plan to build our own GMP gene therapy manufacturing plant;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- continue to establish Medical Affairs field teams to initiate relevant disease education;
- continue to establish a marketing and distribution infrastructure and field force to commercialize our products and any product candidates for which we may obtain marketing approval;
- continue to manage our international subsidiaries and establish new ones;
- continue to operate as a public company and comply with legal, accounting and other regulatory requirements;
- seek to identify, assess, license, acquire, and/or develop other product candidates, technologies, and/or businesses;
- make milestone or other payments under any license or other 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 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, inspection outcomes, 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.

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 are just starting to generate revenue from product sales.

Our ability to generate significant revenue from product sales depends on our ability, alone or with strategic collaboration partners, to successfully commercialize our products and to complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize, one or more of our product candidates. 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:

- obtaining regulatory and marketing approvals with broad indications for product candidates for which we complete clinical studies;

- developing a sustainable and scalable manufacturing process for our products and 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 market demand for our products and product candidates, if approved;
- launching and commercializing our products and product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our products and product candidates as viable treatment options;
- obtaining adequate market share, reimbursement and pricing for our products and product candidates;
- our ability to sell our products and product candidates on a named patient basis or through an equivalent mechanism and the amount of revenue generated from such sales;
- our ability to find patients so they can be diagnosed and begin receiving treatment;
- addressing any competing technological and market developments;
- negotiating favorable terms, including commercial rights, in any collaboration, licensing, or other arrangements into which we may enter, any amendments thereto or extensions thereof;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

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 our products, even if they receive regulatory approval.

We expect we may need to raise additional capital to fund our activities. This additional financing may not be available on acceptable terms, if 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.

As of December 31, 2019, our available cash, cash equivalents, and investments were $760.4 million. We expect we may need additional capital to continue to commercialize our products, and to develop and obtain regulatory approval for, and to commercialize, all of 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 and commercial supplies of our products and product candidates;
- the cost of creating additional infrastructure, including facilities and systems;
- the number and characteristics of the product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing and operating our international subsidiaries;
- the cost and timing of establishing and operating field forces, marketing, and distribution capabilities;
- the cost and timing of other activities needed to commercialize our products; and
- the terms and timing of any collaborative, licensing, acquisition (including whether we exercise our option to acquire GeneTx pursuant to the terms of our Unitholder Option Agreement with them), and other arrangements that we may establish, including any required milestone, royalty, and reimbursements or other payments thereunder.

Any additional fundraising efforts may divert our management's attention from their day-to-day activities, which may adversely affect our ability to develop our product candidates and commercialize our products. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. 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. If we incur debt, it 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 have in the past sought and may in the future seek funds through a sale of future royalty payments similar to our transaction with Royalty Pharma or through collaborative partnerships, strategic alliances, and licensing or other arrangements and we may be required to relinquish rights to some of our technologies or product candidates, future revenue streams, research programs, and other 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 or at all, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of our products and any approved 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

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. The safety or efficacy results generated to date in clinical studies do not ensure that later clinical studies will demonstrate similar results. For example, our Phase 3 studies that evaluated Ace-ER in patients with GNE myopathy and UX007 in patients with Glut1 DS experiencing disabling paroxysmal movement disorders did not achieve their primary or secondary endpoints. 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 patients 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. We have in the past, and may in the future elect to review interim clinical data at multiple time points during the studies, which could introduce bias into the study results and potentially result in denial of approval.

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:

- delays or failures in generating 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;
- failure to demonstrate a starting dose for our product candidates in the clinic that might be reasonably expected to result in a clinical benefit;
- delays or failures in developing gene therapy, messenger RNA (mRNA), DNA, small interfering RNA (siRNA) or other novel and complex product candidates, which are expensive and difficult to develop and manufacture;
- delays resulting from a shutdown, or uncertainty surrounding the potential for future shutdowns of the U.S. government, including the FDA;
- delays or failures in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with contract research organizations, or CROs, clinical study sites, and other clinical trial-related vendors;

- failure or delays in obtaining required regulatory agency approval and/or IRB or EC approval at each clinical study site or in certain countries;
- failure to correctly design clinical studies which may result in those studies failing to meet their endpoints or the expectations of regulatory agencies;
- changes in clinical study design or development strategy resulting in delays related to obtaining approvals from IRBs or ECs and/or regulatory agencies to proceed with clinical studies;
- 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 and/or ICH'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;
- adverse events associated with the product candidate occurring that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- greater than anticipated costs associated with clinical studies of our drug candidates;
- 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, we may need to conduct additional toxicology, comparability or other studies to bridge our modified product candidates to earlier versions. Clinical study delays could also shorten any periods during which our products have commercial exclusivity 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.

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 timing of patient dosing, the submission or acceptance 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 from our estimates. If we do not meet these publicly announced milestones, 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.

We may find it difficult to identify and 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 example,

- we estimate that approximately 8,000 patients in the developed world suffer from late-onset OTC deficiency, for which DTX301 is being studied, and these all may not be treatable if they are immune to the virus; and
- we estimate that approximately 6,000 patients worldwide suffer from GSDIa, for which DTX401 is being studied, and these all may not be treatable if they are immune to the virus.

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 patients to 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. The process of finding and diagnosing patients may prove costly, especially since the rare diseases we are studying are commonly under diagnosed. We also may not be able to identify, recruit, and enroll a sufficient number of appropriate patients to complete our clinical studies because of demographic criteria for prospective patients, 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. 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. Furthermore, 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. 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.

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 commercialize our products and 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. We have only obtained regulatory approval for two products, 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 (including good clinical practices), 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, positions of the regulatory agencies on study design and/or endpoints, 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 be denied. 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:

- regulatory authorities may disagree with the design, implementation, or conduct of our clinical studies;
- regulatory authorities may change their guidance or requirements for a development program for a product candidate;
- 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;
- 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 biologics license application, or BLA, or other submission or to obtain regulatory approval;
- we may be unable to demonstrate to regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities used to manufacture our clinical and commercial supplies;
- the U.S. government may be shut down, which could delay the FDA;

- failure of our nonclinical or clinical development to comply with an agreed upon Pediatric Investigational Plan (PIP), which details the designs and completion timelines for nonclinical and clinical studies and is a condition of marketing authorization in the EU; and
- the approval policies or regulations of 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. Additionally, many of the disease states we are targeting, such as LC-FAOD, are highly heterogeneous in nature, which may impact our ability to determine the treatment benefit of our potential therapies.

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

The regulatory approval process for novel product candidates, such as our gene therapy product candidates, can be more expensive and take longer than for other product candidates, and may change in the future.

The clinical trial requirements of regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. As a result, the regulatory approval process for novel product candidates such as our gene therapy product candidates can be more expensive and take longer than for other, better known or more extensively studied product candidates, which can lead to fewer product approvals. To date, very few gene therapy products have received regulatory approval in the United States or Europe.

Additionally, the FDA, Health Canada, and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA, which governs the development of gene therapies in the EU and may issue new guidelines concerning the development and marketing authorization for gene therapy products, advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as U.S. congressional committees and foreign governments, have also expressed interest in further regulating the biotechnology industry. Different regulatory approaches by jurisdiction can result in different or additional preclinical studies or clinical trials being required to support regulatory approval in each jurisdiction.

Regulatory requirements such as review committees and advisory groups, the new guidelines they promulgate, and new guidance issued by regulatory authorities may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post- approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

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, the delay or denial of regulatory approval by the FDA or other comparable foreign authorities, or 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. Our product candidates are in development and the safety profile has not been established. For example, in a completed Phase 2 study, LC-FAOD patients treated with UX007 experienced treatment-related adverse events, the most common of which were diarrhea, abdominal/gastrointestinal pain, nausea, and vomiting. There was one treatment-related serious adverse event of moderate gastroenteritis with vomiting. There were two deaths during the LC-FAOD extension study, both deemed to be related to disease progression and not due to treatment with UX007. Gene therapy product candidates using AAV vectors, like DTX301, have been associated with immunologic reaction to the capsid protein or gene at early time points after administration. For example, in our discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B, we observed elevated laboratory alanine transaminase levels, or ALTs. In previous clinical trials involving AAV viral vectors for gene therapy, some subjects experienced adverse events, including the development of a T-cell mediated immune response against the vector capsid proteins. In addition, theoretical side effects of AAV vectors include replication and spread of the virus to other parts of the body and insertional oncogenesis, which is the process whereby the insertion of a gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation or cancer. Potential procedure-related events are similar to those associated with standard coronary diagnostic procedures, and may include vascular injury (e.g., damage to the femoral, radial or brachial arteries at the site of vascular access, or damage to the coronary arteries) or myocardial injury. Future product candidates may also cause these or similar side effects as 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 a study. Such side effects could also 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, even though we received regulatory approval for Crysvita and Mepsevii and even if our product candidates receive marketing approval in the future, if 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 REMS plan;
- 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.

Serious adverse events in clinical trials involving gene therapy product candidates may damage public perception of the safety of our product candidates, increase government regulation, and adversely affect our ability to obtain regulatory approvals for our product candidates or conduct our business.

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. For example, earlier gene therapy trials using other vectors led to several well- publicized adverse events, including cases of leukemia and death. The risk of cancer remains a concern for gene therapy and we cannot assure you that it will not occur in any of our planned or future clinical studies. In addition, there is the

potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products, particularly AAV gene therapy products such as candidates based on the same capsid serotypes as our product candidates, or occurring during use of our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our gene therapy product candidates, stricter labeling requirements for those gene therapy product candidates that are approved and a decrease in demand for any such gene therapy product candidates, all of which would have an adverse effect on our business, financial condition, results of operations and prospects.

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

Our products and any product candidates that are approved are 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 Good Manufacturing Practices (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 4 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 was 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 promote our products only for indications or uses for which they 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.

If we are unable to identify, source, and develop effective biomarkers, or our collaborators are unable to successfully develop and commercialize companion diagnostics for our product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

We are developing companion diagnostic tests to identify the right patients for certain of our product candidates and to monitor response to treatment. In certain cases, diagnostic tests may need to be developed as companion diagnostics and regulatory approval obtained in order to commercialize some product candidates. We currently use and expect to continue to use biomarkers to identify the right patients for certain of our product candidates. We may also need to develop predictive biomarkers in the future. For example, to evaluate therapeutic response of DTX301, we are measuring ammonia levels and other biomarkers, including ^{13}C-acetate, which are established measures of OTC deficiency disease status and ureagenesis. We offer no assurances that ^{13}C-acetate or any other future potential biomarker will in fact prove predictive, be reliably measured, or be accepted as a measure of efficacy by the FDA or other regulatory authorities. In addition, our success may depend, in part, on the development and commercialization of companion diagnostics. We also expect the FDA will require the development and regulatory approval of a companion diagnostic assay as a condition to approval of our gene therapy product candidates. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostics. Development and manufacturing of companion diagnostics is complex and there are limited manufacturers with the necessary expertise and capability. Even if we are able to find a qualified collaborator, it may not be able to manufacture the companion diagnostics at a cost or in quantities or on timelines necessary for use with our product candidates. To be successful, we need to address a number of scientific, technical and logistical challenges. We have not yet initiated development and commercialization of companion diagnostics. We have little experience in the development and commercialization of diagnostics and may not be successful in developing and commercializing appropriate diagnostics to pair with any of our product candidates that receive marketing approval. University of Pennsylvania School of Medicine currently conducts some of our clinical assays pursuant to a sponsored research agreement, one of which is required for our ongoing Phase 1/2 clinical trial. We also use third parties for the automation, characterization and validation, of our bioanalytical assays, companion diagnostics and the manufacture of its critical reagents.

Companion diagnostics are subject to regulation by FDA and similar regulatory authorities outside the United States as medical devices and require regulatory clearance or approval prior to commercialization. In the United States, companion diagnostics are cleared or approved through FDA's 510(k) premarket notification or premarket approval, or PMA, process. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted 510(k) premarket notification, PMA or equivalent application types in jurisdictions outside the United States, may cause delays in the approval, clearance or rejection of an application. Given our limited experience in developing and commercializing diagnostics, we expect to rely in part or in whole on third parties for companion diagnostic design and commercialization. We and our collaborators may encounter difficulties in developing and obtaining approval or clearance for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by us or our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates.

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, collaborative partners, and independent investigators 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, pursuant to the terms of our collaboration with GeneTx on the development of GeneTx's GTX-102, an antisense oligonucleotide (ASO) for the treatment of Angelman syndrome, subject to certain limited rights we have, GeneTx retains the decision-making authority on all matters in connection with the research, development, manufacturing and regulatory activities with respect to the program. With respect to our collaboration with Arcturus, we rely on our partner Arcturus for the design and optimization of initial product candidates under our mRNA, DNA and siRNA collaborations. 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 European Economic Area, 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, including the sites at which clinical studies are conducted, 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 deny approval and/or 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 the regulatory authorities determine that we have failed to comply with GLP, GMP, or GCP regulations, they may deny approval of our product candidates and/or 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 efforts to support patient diagnosis and identify patients, 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 KKC for the clinical and commercial supply of Crysvita for all major markets and for the development and commercialization of Crysvita in certain major markets, and KKC's failure to provide an adequate supply of Crysvita or to commercialize Crysvita in those markets could result in a material adverse effect on our business and operating results.

Under our agreement with KKC, KKC has the sole right to commercialize Crysvita in Europe and, at a specified time, in the United States, Canada, and Turkey, subject to a limited promotion right we retained. Our partnership with KKC 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:

- KKC has no obligation under our agreement to use diligent efforts to commercialize Crysvita in Europe. The timing and amount of any royalty payments that are made by KKC based on sales of Crysvita in Europe will depend on, among other things, the efforts, allocation of resources, and successful commercialization of Crysvita by KKC in Europe.
- the timing and amount of any payments we may receive under our agreement with KKC will depend on, among other things, the efforts, allocation of resources, and successful commercialization of Crysvita by KKC in the United States and Canada under our agreement;
- KKC may change the focus of its commercialization efforts or pursue higher-priority programs;
- KKC may make decisions regarding the indications for our product candidates in countries where it has the sole right to commercialize the product candidates that limit commercialization efforts in those countries or in countries where we have the right to commercialize our product candidates;
- KKC may make decisions regarding market access and pricing in countries where it has the sole right to commercialize our product candidates which can negatively impact our commercialization efforts in countries where we have the right to commercialize our product candidates;
- KKC may fail to manufacture or supply sufficient drug product of Crysvita in compliance with applicable laws and regulations or otherwise for our development and clinical use, which could result in program delays;
- KKC may fail to manufacture or supply sufficient drug product of Crysvita in compliance with applicable laws and regulations or otherwise for our commercial use, which could result in lost revenue;
- KKC may elect to develop and commercialize Crysvita indications with a larger market than XLH and at a lower price, thereby reducing the profit margin on sales of Crysvita for any orphan indications, including XLH;
- if KKC were to breach or terminate the agreement with us, we would no longer have any rights to develop or commercialize Crysvita or such rights would be limited to non-terminated countries;
- KKC 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 KKC may be greater than anticipated.

We rely on third parties to manufacture our products and most of our product candidates and to acquire the raw material components to manufacture such products and 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 cost.

We have limited infrastructure or capability internally to manufacture our products and product candidates, and we currently lack the resources and the capability to manufacture our products and most 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 products and 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 products and our product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We also do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. We may also experience interruptions in supply of product if the product or raw material components fail to meet our quality control standards or the quality control standards of our suppliers. Any significant interruption in the supply of products due to delays in obtaining the raw material components or for other reasons could hinder our ability to distribute products to meet commercial demand and negatively impact our business. 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, among other things, the failure of a manufacturer to provide a drug substance or drug product of sufficient quantity or quality, or 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 have no experience as a company developing a manufacturing facility and may not be able to do so successfully if we determine to expand or develop our manufacturing capability and infrastructure.

We expect our future manufacturing strategy to involve the use of one or more CMOs as well as our own capabilities and infrastructure, including at our Woburn, MA facility or new facilities we may develop. We expect that development of our own process development facility will provide us with enhanced control of material supply for both clinical trials and the commercial market, enable the more rapid implementation of process changes, and allow for better long-term margins. However, we have no experience as a company in developing a manufacturing facility and may never be successful in developing our own manufacturing facility or capability. Additionally, given that cGMP gene therapy manufacturing is a nascent industry, there are a small number of CMOs with the experience necessary to manufacture our gene therapy product candidates and we may have difficulty finding or maintaining relationships with such CMOs or hiring experts for internal manufacturing and accordingly, our production capacity may be limited. We may establish multiple manufacturing facilities as we expand our commercial footprint to multiple geographies, which may lead to regulatory delays or prove costly. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, lack of capacity, labor shortages, natural disasters, power failures, program failures, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

Gene therapy and mRNA, DNA and siRNA product candidates are novel, complex, expensive and difficult to manufacture. We could experience manufacturing problems that result in delays in developing and commercializing these programs or otherwise harm our business.

The manufacturing process used to produce our gene therapy, mRNA, DNA and siRNA product candidates is novel, complex, and has not been validated for commercial use. Several factors could cause production interruptions, including equipment malfunctions, regulatory inspections, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Our gene therapy, mRNA, DNA and siRNA product candidates require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of a biologic such as gene therapy, mRNA, DNA and siRNA product candidates generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate is consistent from lot to lot or will perform in the intended manner. Accordingly, we employ multiple steps to control the manufacturing process to assure that the process works reproducibly and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, noncompliance with regulatory requirements, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate the manufacturing processes for our gene therapy, mRNA, DNA and siRNA product candidates, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements. We may be unable to scale up existing or new facilities, including our facility in Woburn, MA, and such facilities may not enable the expansion of our internal manufacturing process discovery and development to the extent we anticipate, or at all.

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

The process of manufacturing our products and product candidates is complex, highly regulated, and subject to several risks, including but not limited to those listed below.

- The process of manufacturing our products and 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 our products and 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 products and product candidates or in the manufacturing facilities in which our products and product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facilities in which our products and product candidates are made could be adversely affected by equipment failures, labor shortages, raw material shortages, natural disasters, power failures, and numerous other factors.

Any adverse developments affecting manufacturing operations for our products and product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our products and product candidates. For instance, during the fourth quarter of 2019, we experienced disruptions from our third party supplier related to the fill and finish activities for the manufacture of Mepsevii, which negatively impacted our inventory of the product. Due to their stage of development, small volume requirements, and infrequency of batch production runs, we carry limited amounts of safety stock for our products and product candidates. We may also have to take inventory write-offs and incur other charges and expenses for products and product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

The drug substance and drug product for our products and 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 necessary drug substance or drug product, could materially and adversely affect our business.

We acquire most of the drug substances and drug products for our products and product candidates from single sources. If any single source supplier breaches an agreement with us, or terminates the agreement in response to an alleged breach by us or otherwise becomes unable to fulfill its supply obligations, we would not be able to manufacture and distribute the product or product candidate until a qualified alternative supplier is identified, which could significantly impair our ability to commercialize such product or delay the development of such product candidate. The drug substance and drug product for Crysvita are made by KKC pursuant to our license and collaboration agreement with KKC. The drug substance and drug product for Mepsevii are manufactured by Rentschler under a commercial supply and services agreement and accompanying purchase orders. The pharmaceutical-grade drug substance for UX007 is manufactured by IOI Oleo pursuant to our supply agreement with IOI Oleo, and the drug product for UX007 is prepared by Haupt Pharma AG and CPM pursuant to purchase orders. Single source suppliers are also used for our gene therapy programs. We have not currently secured any other suppliers for the drug substance or drug product of our products and 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 expense or delay in the commercialization of our products or the development of our product candidates. For instance, we have recently experienced disruptions from our third-party supplier related to the fill and finish activities for the manufacture of Mepsevii and as a result, we are in the process of identifying an alternative supplier to conduct such activities. It may take a significant amount of time and expense to qualify an alternative supplier, once identified, and to transfer activities to such supplier. If we fail to identify and qualify an alternative supplier in a timely manner, we could experience delays or disruptions in the supply of Mepsevii, which would negatively impact sales of the product. Additionally, we may not be able to enter into supply arrangements with alternative suppliers on commercially reasonable terms or at all. The terms of any new agreement, such as any agreement with our alternative supplier for Mepsevii, may also be less favorable or more costly than the terms we have with our current supplier. A delay in the commercialization of our products or 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 on our business.

We and our collaborators and contract manufacturers are subject to significant regulation with respect to manufacturing our products and 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 and collaboration partners for our product and 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 products and 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 products, 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 cannot schedule manufacturing to meet inspectional demands or do not initially pass and continue to pass regulatory inspections, including pre-approval plant inspections, regulatory approval of our product candidates 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, such as KKC, 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, recalls or seizures of product or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us, our collaborators, or third parties with whom we contract could materially harm our business.

If we, our collaborators, including KKC, 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 interruptions in the supply of our products or a 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, we could experience supply interruptions of product that would impact our ability to meet commercial demand and result in loss of revenue, or our clinical studies may be delayed, which could delay regulatory approval for our product candidates, any and all of which could materially and adversely affect our business.

The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such distributors and specialty pharmacies could adversely affect our revenues, financial condition, or results of operations.

We rely on commercial distributors and specialty pharmacies for a considerable portion of our product sales and such sales are concentrated within a small number of distributors and specialty pharmacies. The financial failure of any of these parties could adversely affect our revenues, financial condition or results of operations. Our revenues, financial condition or results of operations may also be affected by fluctuations in buying or distribution patterns of such distributors and specialty pharmacies. These fluctuations may result from seasonality, pricing, wholesaler inventory objectives, or other factors.

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 in connection with the development and manufacture of our products and product candidates and will likely rely on third parties in connection with the commercialization of our approved products, 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 Products and Product Candidates

If the market opportunities for our products and 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 products and 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 that may reduce the penetration of Crysvita 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 products and 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 products and 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 products and product candidates may be limited or may not be amenable to treatment with our products and product candidates, and new patients may become increasingly difficult to identify or access, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our products and 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.

Manufacturers that produce our products and product candidates may not have experience producing our products and product candidates at commercial levels and may not achieve the necessary regulatory approvals or produce our products and product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization.

We rely on third-party manufacturers to produce our products and product candidates. These manufacturers may not have the experience or ability to produce our products and 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 for all of our product candidates. If our manufacturing partners are not able to conduct all such necessary activities in accordance with applicable regulations, our commercialization efforts will be harmed. We have not yet secured manufacturing capabilities for commercial quantities of all of our product candidates and may be unable to negotiate binding agreements with manufacturers to support our commercialization activities on commercially reasonable terms.

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 products and product candidates, are unable to comply with GMP or other pertinent regulatory requirements, or are unable to produce our products and product candidates within our planned timeframe and cost parameters, the development and sales of our products and product candidates, if approved, may be materially harmed.

Additionally, the cost to us for the supply of our products and product candidates manufactured by such third parties may be high and could limit our profitability, even if our third-party product manufacturers develop acceptable manufacturing processes that provide the necessary quantities of our products and product candidates in a compliant and timely manner. Furthermore, KKC is our sole supplier of commercial quantities of Crysvita. The supply price to us for commercial sales of Crysvita in the United States, Canada and in Latin America, which is 35% of net sales through December 31, 2022 and 30% thereafter, is 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 treatments that may compete with our products and product candidates. For example, XLH is treated with oral phosphate and vitamin D therapy, which may compete with Crysvita; LC-FAOD is managed with diet therapy and medium-chain triglyceride oil, which may compete with UX007; OTC deficiency is currently treated with nitrogen scavenging drugs and severe limitations in dietary protein, which may compete with DTX30; and GSDIa is currently treated with corn starch, which may compete with DTX401. Triheptanoin is available in food-grade form, which may compete with our pharmaceutical-grade product. Furthermore, investigator-sponsored trials evaluating triheptanoin in multiple indications are ongoing. 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, biotechnology companies, startups, academic research institutions, government agencies, and public and private research institutions. 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 products and product candidates uneconomical or obsolete, and we may not be successful in marketing our products and product candidates against competitors.

We continue to build and evolve an integrated commercial organization. If we are unable to expand our existing commercial infrastructure or enter into agreements with third parties to market and sell our products and product candidates, as needed, we may be unable to generate significant revenue.

In order to successfully commercialize Crysvita and Mepsevii as well as any additional products that may result from our development programs, we are building a commercial infrastructure in North America, Europe and Latin America. This infrastructure consists of both office based as well as field teams with technical expertise, and will be expanded as we approach the potential approval dates of additional products that result from our development programs. This will be expensive and time consuming. Any failure or delay in the expansion of this infrastructure may adversely impact the commercialization of our approved products.

Although our employees may have promoted other similar products in the past while employed at other companies, we, as a company, have limited, recent experience selling and marketing our product. Further, given our limited 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 products and product candidates or we may incur excess costs in an effort to optimize the hiring of commercial personnel. 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 a large 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.

Our exclusive right to promote Crysvita in the United States and Canada expires in 2023.

Pursuant to the terms of our collaboration and license agreement with KKC, we have the sole right to promote Crysvita in the United States and Canada, or the profit-share territory, until the transition date of April 2023, which is the fifth anniversary of the commercial launch of the product in the United States. After the transition date, KKC will have the right to promote the product, subject to a limited promotion right retained by us. Although we expect that we will use our North America commercial infrastructure to promote our other commercialized products after the transition date, we cannot assure that we will have adequate commercial activity to support our field force and other aspects of our commercial infrastructure in the territory. After the transition date, we will also solely bear the expenses related to the promotion of Crysvita in the profit-share territory pursuant to our limited promotion right, rather than share such expenses with KKC. We expect to collaborate with KKC to provide for a seamless transition of responsibilities for KKC to promote the product in the profit-share territory after the transition date, however, the commercial success of Crysvita in the profit-share territory after the transition date will depend on, among other things, the efforts and allocation of resources of KKC.

The commercial success of any current or future product 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 current and future products will depend in part on the medical community, patients, and payors accepting our current and future products 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 current and future products 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 current and future products 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 products and 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. We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial, when and if they achieve regulatory approval. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to afford expensive treatments such as ours, assuming approval. Sales of our products and product candidates, if approved, will depend substantially, both domestically and abroad, on the extent to which their costs 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, are available only to limited levels, or are not available on a timely basis, we may not be able to successfully commercialize our products and product candidates, if approved. For example, deteriorating economic conditions and political instability in certain Latin American countries and in Turkey may cause us to experience significant delays in receiving approval for reimbursement for our products and consequently impact our product commercialization timelines in such regions. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to sustain our overall enterprise.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, 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 or private payors will decide with respect to reimbursement for products such as ours, especially our gene therapy product candidates as there is a limited body of established practices and precedents for gene therapy products.

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 products and 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 and, as a result, they may not cover or provide adequate payment for our products and product candidates. We expect to experience pricing pressures in connection with the sale of any of our products and product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, additional legislative changes, and statements by elected officials. For example, proposals are being discussed to tie U.S. drug prices to the cost in other countries, 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, and with respect to prescription drugs, surgical procedures, and other treatments in particular, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

The results of the United Kingdom’s referendum on withdrawal from the EU may have a negative effect on our business, global economic conditions, and financial markets.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. On January 30, 2020, the United Kingdom formally withdrew from the EU. Following the United Kingdom’s formal withdrawal from the EU, the United Kingdom will to continue to follow all of the EU’s rules and its trading relationship with the EU will remain the same during a transition period which will expire on December 31, 2020. Several aspects of the United Kingdom and EU relationship will need to be determined during the transition period, including free trade agreements and rules and regulations affecting the biotechnology or pharmaceutical industries. Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of product candidates, disrupt the manufacture of our products and product candidates in the United Kingdom or the EU, disrupt the importation and export of active substances and other components of drug formulations, and disrupt the supply chain for clinical trial product and final authorized formulations. Any delay in obtaining, or an inability to obtain, any marketing approvals, or disruption to our and our collaborators’ supply chain as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. The cumulative effect of disruptions to the regulatory framework or supply chains may add considerably to the development lead time to, and expense of, marketing authorization and commercialization of products in the EU and/or the United Kingdom. In view of the uncertainty surrounding the Brexit implementation, we are unable to predict the effects of such disruption to the regulatory framework and supply chain in Europe.

Further, these developments, or the perception that any of them could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU laws to replace or replicate following the expiration of the transition period, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs and depress economic activity. In addition, we expect that Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which EU laws to replicate or replace. We are taking certain precautionary measures with respect to Brexit and its impact to the EU, and will continue to monitor the situation. If the United Kingdom were to significantly alter its regulations affecting the biotechnology or pharmaceutical industries, we could face significant new costs. It may also be time-consuming and expensive for us to alter our internal operations in order to comply with new regulations. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and affect our strategy in the U.K. and EU biotech market.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain effective patent rights for our products, 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, our products, and our 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, our products, and our product candidates.

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 products or 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 products or 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 the patents and patent applications we own or in-license are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our products or 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 products or 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 products and product candidates in all territories. For example, there are no issued patents covering the Crysvita composition of matter in Latin America where we have rights to commercialize the compound. Therefore, a competitor could develop the same antibody or a similar antibody as well as other approaches that target FGF23 for potential commercialization in Latin America, subject to any intellectual property rights or regulatory exclusivities awarded to us. If we cannot obtain and maintain effective patent rights for our products or 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 its effective filing date. 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 Crysvita, Mepsevii, UX007, DTX301, and DTX401, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. Furthermore, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we do not have sufficient patent terms or regulatory exclusivity to protect our products, our business and results of operations may 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 16, 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 also moved to a first to file system. The Leahy-Smith Act included a number of significant changes that affect the way patent applications are prosecuted and the way patents can be challenged. The effects of these changes are currently unclear as the courts have only begun to address these provisions. 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 products, 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 products or 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, *inter partes* reviews, post grant reviews, 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 products or 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 products or product candidates. We have conducted freedom to operate analyses with respect only to our products and 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 products or 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 products or product candidates may infringe.

We are aware of four third-party patent families that include issued U.S. patents with claims that, if valid and enforceable, could be construed to cover one or more of our gene therapy product candidates, if and when approved, or methods of their manufacture. We are also aware of two third-party patent families that include issued European claims that, if valid and enforceable, could be construed to cover certain methods that may be used in the manufacture of one or more of our gene therapy product candidates. 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 our products or 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 our products or a 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 continue commercialization of our products, or block our ability to 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 commercialize 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 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 Crysvita, Mepsevii, DTX301, and DTX401.

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 Crysvita, Mepsevii, DTX301, and DTX401. In the United States, the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, was included in the Affordable Care Act and 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. Moreover, it is not known whether the BPCI Act will survive in whole or in part if the Affordable Care Act is repealed by Congress or held unconstitutional by courts. As a result, its ultimate impact, implementation, meaning, and long-term existence are subject to uncertainty. Elimination or modification of the BPCI Act, or changes to the FDA's interpretation or implementation of the BPCI Act, could have a material adverse effect on the future commercial prospects for Crysvita, Mepsevii, DTX301, and DTX401.

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 or future small-molecule product candidates.

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, and 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 enforce its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if UX007 is approved, competitors could file ANDAs for generic versions of UX007, or 505(b)(2) NDAs that reference UX007. If there are patents listed for UX007 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 KKC, who is primarily responsible for the prosecution of patents and patent applications licensed to us under the collaboration agreement.

In addition, we have in-licensed patents and patent applications owned by the University of Pennsylvania, relating to the AAV8 vector used in DTX301 and DTX401. These patents and patent applications are licensed or sublicensed by REGENXBIO and sublicensed to us. We do not have the right to control the prosecution of these patent applications, or the maintenance of any of these patents. In addition, under our agreement with REGENXBIO, we do not have the first right to enforce the licensed patents, and our enforcement rights are subject to certain limitations that may adversely impact our ability to use the licensed patents to exclude others from commercializing competitive products. Moreover, REGENXBIO and the University of Pennsylvania may have interests which differ from ours in determining whether and the manner in which to enforce such patents.

If KKC, the University of Pennsylvania, or any of our future licensing partners fail to appropriately prosecute, maintain, and enforce patent protection for the 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 and Collaboration Agreements" above for a description of our license agreements with KKC, Baylor Research Institute, Saint Louis University, Bayer, REGENXBIO, and the University of Pennsylvania, which include descriptions of the termination provisions of these agreements.

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 intellectual property 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 intellectual property litigation, if we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering our products or one of our product candidates, the defendant could counterclaim that the patent covering our product or 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 or derivation proceedings now available under the Leahy-Smith Act provoked by third parties or brought by us or declared or instituted 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. In addition, the validity of our patents could be challenged in the USPTO by one of the new post grant proceedings (*i.e., inter partes* review or post grant review) now available under the Leahy-Smith Act. Our defense of litigation, interference proceedings, or post grant proceedings under the Leahy-Smith Act 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 distract 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 to successfully defend against 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 distract 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 biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involves both technological and legal complexity. Therefore, obtaining and enforcing such 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. For example, in *Association for Molecular Pathology v. Myriad Genetics*, *Inc.*, the Supreme Court ruled that a "naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," invalidating Myriad Genetics' patents on the BRCA1 and BRCA2 genes. Certain claims of our licensed U.S. patents covering DTX301 and DTX401 relate to isolated AAV8 vectors, capsid proteins, or nucleic acids. To the extent that such claims are deemed to be directed to natural products, or to lack an inventive concept above and beyond an isolated natural product, a court may decide the claims are invalid under *Myriad*. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, 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 our products or 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 KKC 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. 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 and for various subtypes of LC-FAOD in Europe, as well as for Crysvita, Mepsevii, DTX301 and DTX401 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 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.

Our operating results would be adversely impacted if our intangible assets become impaired.

As a result of the accounting for our acquisition of Dimension Therapeutics, Inc. (Dimension) in November 2017, we have recorded on our balance sheet intangible assets for in-process research and development ("IPR&D") related to DTX301 and DTX401. We test the intangible assets for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired. If the associated research and development effort is abandoned, the related assets will be written-off and we will record a noncash impairment loss on our statement of operations. We have not recorded any impairments related to our intangible assets through the end of December 31, 2019.

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, require 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 technical, financial or human 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 research, discovery, 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 may expend our limited resources to pursue a particular product, product candidate or indication and fail to capitalize on products, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus our sales, marketing and research programs on certain products, product candidates or for specific indications. As a result, we may forego or delay pursuit of opportunities with other

products or product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product or product candidate, we may relinquish valuable rights through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If we are unable to maintain and further develop effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our stock may decrease.

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 also subject to the compliance requirements of Section 404(b) of the Sarbanes-Oxley Act, which results in us incurring substantial expenses and expending significant management efforts. We currently do not have a separate internal audit group. We may 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 or our independent registered public accounting firm identify deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, investors may lose confidence in the accuracy and completeness of our financial reports, 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, the Affordable Care Act, as amended, substantially changed the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, 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, and establishes annual fees and taxes on manufacturers of certain branded prescription drugs. A federal district court ruled the entire Affordable Care Act to be unconstitutional in December 2018, but issued a stay, meaning the law will remain in effect while the ruling is appealed. Implementation of the Affordable Care Act remains ongoing, but there is uncertainty as to how the law's various provisions will ultimately affect the industry and whether the law will remain in place.

Other legislative changes have been adopted in the United States, including the Cures Act and the Budget Control Act of 2011, or the Budget Act, signed into law on August 2, 2011. The Cures Act introduced a wide range of reforms and the Budget Act, 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. In 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 has been extended to 2025.

We expect that additional state and federal healthcare reform measures and regulations will be adopted in the future, including proposals to reduce the exclusivity protections provided to already approved biological products and to provide biosimilar and interchangeable biologic products an easier path to approval. Any of these measures and regulations could limit the amounts that federal and state governments will pay for healthcare products and services, result in reduced demand for our product candidates or additional pricing pressures and affect our product development, testing, marketing approvals and post-market activities.

EU

In the EU, the European Commission has adopted detailed rules for the safety features appearing on the packaging of medicinal products for human use. The regulations set forth 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 at the adoption of notices and guidelines which will serve the interpretation of currently applicable regulations and directives. For example, between August 2015 and December 2016, the European Commission launched public consultations which concerned good manufacturing practices, clinical trials for human medicinal products, and orphan medicinal products. The purpose of the consultation on orphan medicinal products (which will be replaced with a Notice) is to streamline the regulatory framework and to adapt the applicable regulations 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 are subject, directly and 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.

Our operations are directly, and 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 impact, among other things, our field marketing and education programs. In addition, we are 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, including the EU General Data Protection Regulation, are described under "Business—Government Regulation" above. Further, in the United States, California recently enacted the California Consumer Privacy Act (CCPA), which became effective on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. 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. 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. We may also incur increased costs as a result of complying with new legislations such as the CCPA.

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.

Our business strategy includes international expansion. We currently conduct clinical studies and regulatory activities and we also commercialize products outside of the United States. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy and data regulations, transparency regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- introduction 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 for, 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 on 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, results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease (including for example, the recent coronavirus outbreak), boycotts, adoption or expansion of government trade restrictions, 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, including those under the U.K. Bribery Act and similar foreign laws and regulations; 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 have a multinational tax structure and are subject to income tax in the United States and various foreign jurisdictions. Our effective tax rate is influenced by many factors including changes in our operating structure, changes in the mix of our earnings among countries, our allocation of profits and losses among our subsidiaries, our intercompany transfer pricing agreements and rules relating to transfer pricing, the availability of U.S. research and development tax credits, and future changes in tax laws and regulations in the U.S. and foreign countries. Significant judgment is required in determining our tax liabilities including management's judgment for uncertain tax positions. The Internal Revenue Service, other domestic taxing authorities, or foreign taxing authorities may disagree with our interpretation of tax laws as applied to our operations. Our reported effective tax rate and after-tax cash flows may be materially and adversely affected by tax assessments in excess of amounts accrued for our financial statements. This could materially increase our future effective tax rate thereby reducing net income and adversely impacting our results of operations for future periods.

Failure to comply with laws and regulations could harm our business and our reputation.

Our business is subject to regulation by various federal, state, local and foreign governmental agencies, including agencies responsible for monitoring and enforcing employment and labor laws, workplace safety, and tax laws and regulations. In certain jurisdictions, these regulatory requirements may be more stringent than those in the United States, and in other circumstances these requirements may be more stringent in the United States. Noncompliance with applicable regulations or requirements could subject us to investigations, sanctions, mandatory recalls, enforcement actions, disgorgement of profits, fines, damages, civil and criminal penalties, or injunctions. If any governmental sanctions, fines or penalties are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, operating results, financial condition and our reputation could be harmed. In addition, responding to any action will likely result in a significant diversion of management's attention and resources and an increase in professional fees. Enforcement actions and sanctions could further harm our business, operating results, financial condition, and our reputation.

In particular, our research and development activities and our 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, such as viruses, and other hazardous compounds, which subjects us to laws and regulations governing such activities. 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. We cannot guarantee that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, 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 multiple years 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, 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 CROs 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. Improper or inadvertent employee behavior, including data privacy breaches by employees and others with permitted access to our systems, may also pose a risk that sensitive data may be exposed to unauthorized persons or to the public. If a system failure or security breach occurs and interrupts our operations or the operations at one of our third-party vendors, it could result in intellectual property and other proprietary or confidential information being lost or stolen or 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, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data, or disruption of the manufacturing process, 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 reputation 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 one of our laboratories are located in the San Francisco Bay Area, and our collaboration partner for Crysvita, KKC, 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 may be inadequate 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.

We may acquire companies or products or engage in strategic transactions, which could divert our management's attention and cause us to incur various costs and expenses.

We may acquire or invest in businesses or products that we believe could complement or expand our business or otherwise offer growth opportunities. For example, we acquired Dimension in November 2017 and during the third quarter 2019, we entered into an agreement with GeneTx to collaborate on the development of a product for the treatment of Angelman Syndrome which included an exclusive option to acquire GeneTx. The pursuit of potential acquisitions or investments may divert the attention of management and may cause us to incur various costs and expenses in identifying, investigating, and pursuing them, whether or not they are consummated. We may not be able to identify desirable acquisitions or investments or be successful in completing or realizing anticipated benefits from such transactions.

In addition, we may receive inquiries relating to potential strategic transactions, including collaborations, licenses, and acquisitions. Such potential transactions may divert the attention of management and may cause us to incur various costs and expenses in investigating and evaluating such transactions, whether or not they are consummated.

Litigation may substantially increase our costs and harm our business.

We have been, and may in the future become, party to lawsuits including, without limitation, actions and proceedings in the ordinary course of business relating to our directors, officers, stockholders, intellectual property, and employment matters, which will cause us to incur legal fees and other costs related thereto, including potential expenses for the reimbursement of legal fees of officers and directors under indemnification obligations. The expense of defending against such litigation may be significant and there can be no assurance that we will be successful in any defense. Further, the amount of time that may be required to resolve such lawsuits is unpredictable, and these actions may divert management's attention from the day-to-day operations of our business, which could adversely affect our business, results of operations, and cash flows. Litigation is subject to inherent uncertainties, and an adverse result in such matters that may arise from time to time could have a material adverse effect on our business, results of operations, and financial condition.

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 products and product candidates;
- decisions by our collaboration partners with respect to the indications for our products and product candidates in countries where they have the right to commercialize the products and product candidates;
- decisions by our collaboration partners regarding market access and pricing in countries where they have the right to commercialize our products and product candidates;
- failure to successfully develop and commercialize our products and product candidates;
- the level of revenue we receive from our commercialized products or 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 products and product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services, or technologies by our competitors;
- changes in or failure to meet or exceed financial projections or other guidance we may provide to the public;
- changes in or failure to meet or exceed the financial projections or other expectations of the investment community;
- the perception of the pharmaceutical industry or our company by the public, legislatures, regulators, and the investment community;
- the perception of the pharmaceutical industry's approach to drug pricing;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partners, or our competitors;
- the integration and performance of any businesses we have acquired or may acquire;
- 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.

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. At December 31, 2019, 2,710,617 shares were available for future grants under the 2014 Plan. Through January 1, 2024, the number of shares available for future grant under the 2014 Plan will automatically increase on January 1 of each year 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.

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. At December 31, 2019, 2,703,237 shares were available for issuance under the 2014 ESPP. Through January 1, 2024, the number of shares available for issuance under the 2014 ESPP will automatically increase on January 1 of each year 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.

Currently we plan to register the increased number of shares available under the 2014 Plan and the 2014 ESPP each 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. 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, or the IRC, 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 federal and state NOL carryforwards in the amount of $7.2 million and a permanent decrease in federal research tax credit carryforwards in the amount of $0.2 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. 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 resolution adopted by the board 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. Further, no stockholder is permitted to cumulate votes at any election of directors because this right is not included in our amended and restated certificate of incorporation.

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.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, or other employees to us or to our stockholders, (3) any action asserting a claim against us arising under the Delaware General Corporation Law or under our amended and restated certificate of incorporation or bylaws, or (4) any action against us asserting a claim governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage such lawsuits against us and our directors, officers, and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, operating results and financial condition.

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

None.

Item 2. ***Properties***

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

We lease approximately 94,000 square feet of office space in Novato, California used primarily for corporate, clinical, regulatory, quality, manufacturing administration, and commercial functions. The leases for approximately 74,000 square feet will expire in December 2024 and the lease for approximately 20,000 square feet will expire in November 2028.

We also lease approximately 63,000 square feet of office space in Brisbane, California. The rental term for this space will expire in June 2026.

We also lease approximately 15,000 square feet of office and laboratory space in Cambridge, Massachusetts. This lease will expire in December 2023.

We also lease approximately 48,200 square feet of laboratory and office space in Woburn, Massachusetts. The lease for approximately 17,600 will expire in March 2021 and the lease for approximately 30,600 will expire in October 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 or government regulators and we may, from time to time, make claims or take legal actions to assert our rights, including claims relating to our directors, officers, stockholders, intellectual property rights, 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.

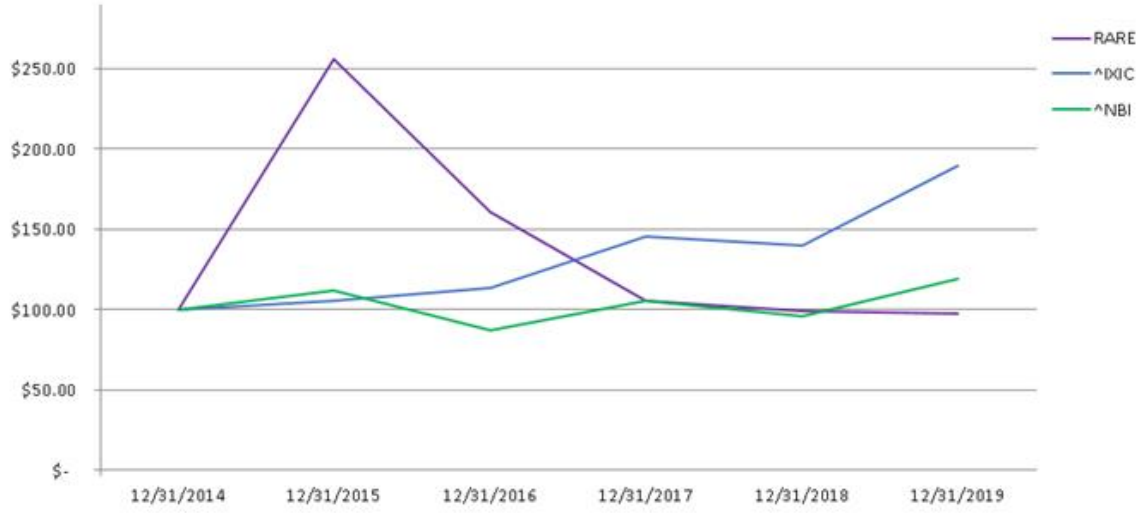
PART II

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". As of February 10, 2020, we had 4 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 December 31, 2014 through December 31, 2019. The figures represented below assume an investment of $100 in our common stock at the closing price of $43.88 on December 31, 2014 and in the Nasdaq Composite Index and the Nasdaq Biotechnology Index on December 31, 2014 and the reinvestment of dividends into shares of common stock. The comparisons in the table are required by the 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	December 31, 2014	December 31, 2015	December 31, 2016	December 31, 2017	December 31, 2018	December 31, 2019
Ultragenyx Pharmaceutical Inc.	RARE	$ 100.00	$ 255.65	$ 160.23	$ 105.70	$ 99.09	$ 97.33
NASDAQ Composite Index	^IXIC	$ 100.00	$ 105.73	$ 113.66	$ 145.76	$ 140.10	$ 189.45
NASDAQ Biotechnology Index	^NBI	$ 100.00	$ 111.42	$ 87.26	$ 105.64	$ 95.79	$ 119.17

Dividend Policy

We have never declared or paid cash dividends on our common stock. 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.

Unregistered Sales of Equity Securities

None

Issuer's Purchases of Equity Securities

None

Item 6. ***Selected Financial Data***

The information set forth below for the five years ended December 31, 2019 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.

	Year Ended December 31,				
	2019	2018	2017	2016	2015
	(in thousands, except share and per share amounts)				
Consolidated Statement of Operations Data:					
Revenues:					
Collaboration and license	$ 83,493	$ 41,693	$ 2,136	$ —	$ —
Product sales	20,221	9,802	476	133	—
Total revenues	103,714	51,495	2,612	133	—
Operating expenses:					
Cost of sales	9,008	1,146	1	—	—
Research and development	357,355	293,998	231,644	183,204	114,737
Selling, general and administrative	161,524	127,724	99,909	64,936	33,001
Total operating expenses	527,887	422,868	331,554	248,140	147,738
Loss from operations	(424,173)	(371,373)	(328,942)	(248,007)	(147,738)
Interest income	13,238	9,542	4,074	3,789	2,320
Gain from sale of priority review vouchers	—	170,322	—	—	—
Change in fair value of investment in Arcturus equity securities	13,413	—	—	—	—
Non-cash interest expense on liability related to the sale of future royalties	(1,135)	—	—	—	—
Other income (expense)	(787)	(5,588)	6,530	(1,621)	(200)
Loss before income taxes	(399,444)	(197,097)	(318,338)	(245,839)	(145,618)
Benefit from (provision for) income taxes	(3,283)	(514)	16,199	(35)	—
Net loss	$ (402,727)	$ (197,611)	$ (302,139)	$ (245,874)	$ (145,618)
Net loss per share, basic and diluted[1]	$ (7.12)	$ (3.97)	$ (7.12)	$ (6.21)	$ (3.96)
Shares used to compute net loss per share, basic and diluted[1]	56,576,885	49,775,223	42,453,135	39,586,908	36,782,603

(1) See Notes 2 and 17 to our audited consolidated financial statements of this Annual Report for an explanation of the calculations of basic and diluted net loss per share attributable to common stockholders.

	As of December 31,				
	2019	2018	2017	2016	2015
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investments	$ 760,404	$ 459,706	$ 244,468	$ 498,111	$ 536,256
Working capital	747,717	447,644	198,569	341,436	422,289
Total assets	1,135,496	719,558	490,753	540,626	559,569
Total stockholders' equity	653,764	608,908	383,454	473,974	531,090

Item 7. ***Management's Discussion and Analysis of Financial Condition and Results of Operations***

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 analysis generally covers our financial condition and results of operations for the year ended December 31, 2019, including year-over-year comparisons versus the year ended December 31, 2018. Our Annual Report on Form 10-K for the year ended December 31, 2018 includes a discussion and analysis of our financial condition and results of operations for the year ended December 31, 2017 in Item 7 of Part II, "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Overview

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

Approved Therapies and Clinical Product Candidates

Our current approved therapies and clinical-stage pipeline consist of three product categories: biologics, small molecules, and gene therapy product candidates.

Our biologic products include approved therapies Crysvita® (burosumab) and Mepsevii® (vestronidase alfa):

- Crysvita is an antibody targeting fibroblast growth factor 23, or FGF23, developed for the treatment of X-linked hypophosphatemia, or XLH, a rare, hereditary, progressive and lifelong musculoskeletal disorder characterized by renal phosphate wasting caused by excess FGF23 production. Crysvita is approved in the United States for the treatment of XLH in adult and pediatric patients six months of age and older, and in Canada for the treatment of XLH in adult and pediatric patients one year of age and older. In the European Union, or the EU, and the United Kingdom, Crysvita is conditionally approved for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing skeletons. The European Medicine Agency, or EMA, has accepted the application submitted by our partner, Kyowa Kirin International, or Kyowa Kirin, to expand the label to include adults with XLH in the EU and the United Kingdom. In Brazil, Crysvita is approved for treatment of XLH in adult and pediatric patients one year of age and older. We have submitted regulatory filings in various other Latin American countries.

  We are collaborating with Kyowa Kirin Co., Ltd., or KKC (formerly Kyowa Hakko Kirin Co., Ltd., or KHK), and Kyowa Kirin, a wholly owned subsidiary of KKC, on the development and commercialization of Crysvita globally.

  Crysvita is also being developed 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, fractures, fatigue, bone and muscle pain, and muscle weakness. We submitted a supplemental Biologics License Application to the U.S. Food and Drug Administration, or FDA, for Crysvita in TIO in December 2019.
- Mepsevii is an intravenous, or IV, enzyme replacement therapy, developed for the treatment of Mucopolysaccharidosis VII, also known as MPS VII or Sly syndrome, a rare lysosomal storage disease that often leads to multi-organ dysfunction, pervasive skeletal disease, and death. Mepsevii is approved in the United States for the treatment of children and adults with MPS VII. In the EU and the United Kingdom, Mepsevii is approved under exceptional circumstances for the treatment of non-neurological manifestations of MPS VII for patients of all ages. In Brazil, Mepsevii is approved for the treatment of MPS VII for patients of all ages.

Our small molecule pipeline includes UX007, which is in clinical development for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD:

- UX007 is a synthetic triglyceride with a specifically designed chemical composition being studied for the treatment of LC-FAOD, which is a set of rare metabolic diseases that prevents the conversion of fat into energy and can cause low blood sugar, muscle rupture, and heart and liver disease. The FDA has accepted our New Drug Application, or NDA for the treatment of LC-FAOD, and has assigned a Prescription Drug User Fee Act, or PDUFA, date of July 31, 2020. We are also continuing discussions with EU regulatory authorities.

Our gene therapy pipeline includes DTX301 and DTX401 in clinical development for the treatment of two diseases:

- DTX301 is an adeno-associated virus 8, or AAV8 gene therapy product candidate designed for the treatment of patients with ornithine transcarbamylase, or OTC, deficiency. OTC is part of the urea cycle, an enzymatic pathway in the liver that converts excess nitrogen, in the form of ammonia, to urea for excretion. OTC deficiency is the most common urea cycle disorder and leads to increased levels of ammonia. Patients with OTC deficiency suffer from acute hyperammonemic episodes that can lead to hospitalization, adverse cognitive and neurological effects, and death. We have reported positive data from the three dose cohorts of the Phase 1/2 study, with up to six responders of the nine patients dosed in the study. A fourth cohort is enrolling three patients at the 1.0 × 10^13 GC/kg dose, using prophylactic steroids, and data from this cohort are expected in the second half of 2020.
- DTX401 is an AAV8 gene therapy clinical candidate for the treatment of patients with glycogen storage disease type Ia, or GSDIa, a disease that arises from a defect in G6Pase, an essential enzyme in glycogen and glucose metabolism. GSDIa is the most common glycogen storage disease. We have reported positive data from the first and second dose cohorts of the Phase 1/2 study, with all patients showing a clinical response with improvements in glucose control and other metabolic parameters compared to baseline. The confirmatory expansion cohort of three patients at the second cohort dose of 6.0 × 10^12 GC/kg dose is ongoing, and we expect data from this cohort in the first half of 2020.

Financial Operations Overview

We are a biopharmaceutical company with a limited operating history. To date, we have invested substantially all of our efforts and financial resources in identifying, acquiring, and developing our products and product candidates, including conducting clinical studies and providing selling, general and administrative support for these operations. To date, we have funded our operations primarily from the sale of equity securities and the sale of certain future royalties.

We have incurred net losses in each year since inception. Our net losses were $402.7 million and $197.6 million for the years ended December 31, 2019 and 2018. Our net loss for the year ended December 31, 2018 includes the gains from the sale of priority review vouchers of $170.3 million, which we received from the FDA in connection with the approval of Crysvita and Mepsevii. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations.

We record revenue from our collaboration and license agreements and from the sale of our two approved products – Crysvita and Mepsevii. In addition, we also record sales of certain products on a “named patient” basis, which are allowed in certain countries prior to regulatory approval. For the years ended December 31, 2019 and 2018, we recorded $83.0 million and $18.2 million, respectively, in collaboration and license revenue for Crysvita sales and $0.5 million and $23.5 million, respectively, for providing certain research and development services under our collaboration and license arrangement with Bayer Healthcare LLC, or Bayer. For the years ended December 31, 2019 and 2018, we recorded $20.2 million and $9.8 million, respectively, in product sales from our approved products and named patient sales in certain countries.

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. generally accepted accounting principles, or 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. We periodically review our estimates as a result of changes in circumstances, facts and experience. The effects of material revisions in estimates are reflected in the financial statements prospectively from the date of the change in estimate. Our significant accounting policies are more fully described in Note 2 to our financial statements included elsewhere in this Annual Report.

We define our critical accounting policies as those accounting principles generally accepted in the United States of America that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply those principles. We believe the critical accounting policies used in the preparation of our financial statements that require significant estimates and judgments are as follows:

Valuation of Acquired Intangible Assets

We have recorded acquired intangible assets related to our acquisition of Dimension Therapeutics, Inc., or Dimension in November 2017. Intangible assets with definite useful lives are amortized over their estimated useful lives or other systematic basis and reviewed for impairment if certain events occur.

Intangible assets related to IPR&D projects are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. During the period the assets are considered indefinite-lived, they will not be amortized but will be tested for impairment. Impairment testing is performed at least annually in the fourth quarter or when a triggering event occurs that could indicate a potential impairment. If the carrying value of the assets is not expected to be recovered, the assets are written down to their estimated fair values with the related impairment charge recognized in our consolidated statements of operations in the period in which the impairment occurs. If and when development is complete, which generally occurs when regulatory approval to market a product is obtained, the associated assets are deemed finite-lived and are amortized over a period that best reflects the economic benefits provided by these assets.

If projects are not successfully developed, our sales and profitability may be adversely affected in future periods. Additionally, the value of the acquired intangible assets, including IPR&D, may become impaired if the underlying projects do not progress as we initially estimated. We believe that the assumptions used in developing our estimates of intangible asset values were reasonable at the time of the acquisition. However, the underlying assumptions used to estimate expected project sales, development costs, profitability, or the events associated with such projects, such as clinical results, may not occur as we estimated at the acquisition date.

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.

Revenue Recognition

Collaboration and License Revenue

We have certain license and collaboration agreements that are within the scope of Accounting Standards Codification (ASC) 808, *Collaborative Agreements*, which provides guidance on the presentation and disclosure of collaborative arrangements. Generally, the classification of transactions under collaborative arrangements is determined based on the nature of contractual terms of the arrangement, along with the nature of the operations of the participants. When our collaborative partner is the principal in the sale transaction with the customer, we record our share of the collaboration profit as collaboration revenue. Funding received related to research and development services and commercialization costs are generally classified as a reduction of research and development expenses and selling, general and administrative expenses, respectively, in the consolidated statement of operations, because the provision of such services for collaborative partners is not considered to be part of our ongoing major or central operations.

We also receive royalty revenues under certain of our license or collaboration agreements in exchange for license of intellectual property. If we do not have any future performance obligations for these license or collaboration agreements, royalty revenue is recorded as the underlying sales occur.

In order to record collaboration revenue, we utilize certain information from our collaboration partners, including revenue from the sale of the product, associated reserves on revenue, and costs incurred for development and sales activities. For the periods covered in the financial statements presented, there have been no significant or material changes to prior period estimates of revenues and expenses.

The terms of our collaboration agreements may contain multiple performance obligations, which may include licenses and research and development activities. We evaluate these agreements under ASC 606, *Revenue from Contracts with Customers*, to determine the distinct performance obligations. We analogize to ASC 606 for the accounting for distinct performance obligations for which there is a customer relationship. Prior to recognizing revenue, we make estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Total consideration may include nonrefundable upfront license fees, payments for research and development activities, reimbursement of certain third-party costs, payments based upon the achievement of specified milestones, and royalty payments based on product sales derived from the collaboration.

If there are multiple distinct performance obligations, we allocate the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or measuring the cost, plus an estimated margin. We estimate the effort to complete the performance obligation and recognize revenue by measuring the progress towards complete satisfaction of the performance obligation using an input measure.

Product Sales

We sell our approved products through a limited number of distributors. Under ASC 606, revenue from product sales is recognized at the point in time when the delivery is made and when title and risk of loss transfers to these distributors. We also recognize revenue from sales of certain products on a “named patient” basis, which are allowed in certain countries prior to the commercial approval of the product. Prior to recognizing revenue, we make estimates of the transaction price, including any variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Product sales are recorded net of estimated government-mandated rebates and chargebacks, estimated product returns, and other deductions.

Provisions for returns and other adjustments are provided for in the period the related revenue is recorded, as estimated by management. These reserves are based on estimates of the amounts earned or to be claimed on the related sales and are reviewed periodically and adjusted as necessary. If actual results vary, we may need to adjust these estimates, which could have an effect on earnings in the period of the adjustment.

Inventory

We expense costs associated with the manufacture of our products prior to regulatory approval. Typically, capitalization of such inventory begins when we have received the regulatory approval of the product. Prior to the FDA approval of Mepsevii in November 2017 and Crysvita in April 2018, manufacturing and related costs were expensed; accordingly, these costs were not capitalized and as a result are not reflected in the costs of sales during the current period. We expect inventory to increase as we produce Mepsevii at costs that reflect the full costs of manufacturing similar biologic products. Similarly, we expect cost of sales to increase in relation to product revenues as we deplete the previously expensed inventories prior to receiving FDA approval.

For the inventory that is being manufactured after regulatory approval, we value inventory at the lower of cost and net realizable value and determine the cost of inventory using the average-cost method. Inventories consist of currently approved products.

We periodically review our inventories for excess amounts or obsolescence and write down obsolete or otherwise unmarketable inventory to the estimated net realizable value.

Investment in Equity Securities

Our investment in equity securities in Arcturus is subject to the equity method of accounting as we have determined that we have significant influence over, but do not control the significant activities of Arcturus. We have elected to apply the fair value option to account for the equity investments in Arcturus at the time the securities were purchased and such securities will continue to be adjusted to fair value at each reporting period. The decision to elect the fair value option is irrevocable and is determined on an instrument by instrument basis. The investment in common stock is accounted for at fair value based upon the current then current stock price. The option to purchase additional stock is accounted for at fair value using the Black-Scholes option pricing method and utilizes the following inputs: stock price, strike price, volatility, risk free interest rate, and expected term. The expected term is the Company’s estimated period to purchase additional stock. The sensitivity of these inputs to the fair value of the equity security is assessed on a periodic basis. The changes in fair value of the equity investment and option to purchase additional stock is included in the Consolidated Statements of Operations.

Liability Related to the Sale of Future Royalties

In December 2019, we entered into a Royalty Purchase Agreement with RPI Finance Trust (RPI), an affiliate of Royalty Pharma. Pursuant to the agreement, RPI paid us $320.0 million in consideration for the Company’s right to receive royalty payments on the net sales of Crysvita in the European Union, the United Kingdom, and Switzerland effective January 1, 2020 under the terms of

our Collaboration and License Agreement with KKC. The agreement with RPI will automatically terminate, and the payment of royalties to RPI will cease, in the event aggregate royalty payments received by RPI are equal to or greater than the capped amount of $608.0 million prior to December 31, 2030, or in the event aggregate royalty payments received by RPI are less than $608.0 million prior to December 31, 2030, when aggregate royalty payments received by RPI are equal to $800.0 million.

As RPI's rate of return is explicitly limited due to the cap on royalties they may receive, proceeds from the transaction was recorded as a liability related to sale of future royalties on the balance sheet. We will amortize $320.0 million, net of transaction costs of $5.8 million using the effective interest method over the estimated life of the arrangement. In order to determine the amortization of the liability, we are required to estimate the total amount of future royalty payments to be received by us and paid to RPI, subject to the capped amount, over the life of the arrangement. The aggregate future estimated royalty payments, less the $314.2 million of net proceeds, will be recorded as non-cash interest expense over the life of the arrangement. Consequently, we estimate an imputed interest on the unamortized portion of the liability and record interest expense relating to the transaction. We will continue to record the royalty revenue rising from the net sales of Crysvita in the applicable European territories as non-cash royalty revenue in our Consolidated Statements of Operations over the term of the arrangement.

We will periodically assess the expected royalty payments using a combination of historical results, internal projections and forecasts from external sources. To the extent future expected royalty payments are greater or less than our initial estimates or the timing of such payments is materially different than its original estimates, we will prospectively adjust the amortization of the liability and the effective interest rate. Through December 31, 2019, our effective annual interest rate was approximately 10.1%.

There are a number of factors that could materially affect the amount and timing of royalty payments from KKC in the applicable European territories, most of which are not within our control. Such factors include, but are not limited to, the success of KKC's sales and promotion of Crysvita, changing standards of care, the introduction of competing products, approval of label expansion for adults, pricing for reimbursement in various European territories, manufacturing or other delays, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of Crysvita, significant changes in foreign exchange rates as the royalty payments are made in U.S. dollars (USD) while significant portions of the underlying European sales of Crysvita are made in currencies other than USD, and other events or circumstances that could result in reduced royalty payments from European sales of Crysvita, all of which would result in a reduction of non-cash royalty revenues and the non-cash interest expense over the life of the arrangement. Conversely, if sales of Crysvita in Europe are more than expected, the non-cash royalty revenues and the non-cash interest expense recorded by us would be greater over the term of the arrangement.

Stock-Based Compensation

Stock-based compensation costs related to equity awards 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 of options, 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 expense will likely increase. The Black-Scholes option-pricing model requires the use of certain subjective assumptions which determine the estimated fair value of stock-based awards.

- *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*— The expected volatility is based on historical volatility over the look-back period corresponding to the expected term.

In addition to the assumptions used in the Black-Scholes option-pricing model, we 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 restricted stock units (RSUs) and performance stock units (PSUs), the fair value is based on the market value of our common stock on the date of grant. Stock-based compensation expense for RSUs is recognized on a straight-line basis over the requisite service period. PSUs are subject to vest only if certain specified criteria are achieved and the employees' continued service with the Company after achievement of the specified criteria. For certain PSUs, the number of PSUs that may vest are also subject to the achievement of certain specified criteria. Compensation expense for PSUs is recognized only after the achievement of the specified criteria is considered probable and recognized on a straight-line basis between the grant date and the expected vest date, with a catch-up for previously unrecognized expense, if any, recognized in the period the achievement criteria is deemed probable.

For the years ended December 31, 2019, 2018, and 2017 stock-based compensation expense was $82.0 million, $80.1 million and $68.0 million, respectively. As of December 31, 2019, we had $133.0 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 2.40 years.

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.

In conjunction with the Dimension acquisition, we recorded a deferred tax liability reflecting the tax impact of the difference between the book basis and tax basis of acquired IPR&D. Such deferred income tax liability was not used to offset deferred tax assets when analyzing our valuation allowance as the acquired IPR&D is considered to have an indefinite life until we complete or abandon development of the acquired IPR&D.

We recognize 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. Our 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.

As of December 31, 2019, our total deferred tax assets were $494.5 million, excluding the deferred tax liability generated from the Dimension acquisition. 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.

Leases

We adopted Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)* as of January 1, 2019 using the modified retrospective method. The results for the year ended December 31, 2019 are presented under ASC 842. The results for the year ended December 31, 2018 and other prior period amounts were not adjusted and continue to be reported in accordance with historical accounting under prior lease guidance, ASC 840, *Leases (Topic 840)*. We also elected the package of practical expedients under the transition guidance that will retain the historical lease classification and initial direct costs for any leases that existed prior to adoption of the new guidance and the practical expedient to not separate lease and non-lease components.

We determine if an arrangement includes a lease at inception. Right-of-use lease assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. The right-of-use lease asset includes any lease payments made and excluded lease incentives. Incremental borrowing rate is used in determining the present value of future payments. We apply a portfolio approach to the property leases to apply an incremental borrowing rate to leases with similar lease terms. The lease terms may include options to extend or terminate the lease. We recognize the options to extend the lease as part of the right-of-use lease assets and lease liabilities only if it is reasonably certain that the option would be exercised. Lease expense for minimum lease payments is recognized on a straight-line basis over the non-cancelable lease term. Prior period amounts have not been adjusted and continue to be reported in accordance with the Company’s historical accounting under previous lease guidance, Topic 840.

As a result of the adoption of the new guidance, as of January 1, 2019, we recorded a right-of-use lease asset of $16.2 million, a short-term lease liability of $4.5 million, and a long-term lease liability of $17.0 million and no cumulative effect adjustment was made to the retained earnings as of the adoption date. In addition, as of the adoption date, we derecognized a net deferred rent obligation of $5.2 million. See Note 9 of our audited consolidated financial statements of this Annual Report for additional information.

Results of Operations

Comparison of Years Ended December 31, 2019 and 2018

Revenues (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Collaboration and license revenue:				
Crysvita collaboration revenue in profit-share territory	$ 74,869	$ 15,334	$ 59,535	388%
Crysvita royalty revenue in European territory	8,120	2,892	5,228	181%
Bayer	504	23,467	(22,963)	(98%)
Total collaboration and license revenue	83,493	41,693	41,800	100%
Product sales:				
Crysvita	4,286	644	3,642	566%
Mepsevii	12,634	7,903	4,731	60%
UX007	3,301	1,255	2,046	163%
Total product sales	20,221	9,802	10,419	106%
Total revenues	$ 103,714	$ 51,495	$ 52,219	101%

Crysvita was approved in the EU and the United Kingdom in November 2017 and in the U.S. in April 2018. For the year ended December 31, 2019, the Company's share of Crysvita collaboration revenue in the profit-share territory increased by $59.5 million, as compared to the prior year. For the year ended December 31, 2019, the Crysvita royalty revenue in the European territory increased by $5.2 million, as compared to the prior year. The increases primarily reflect the continuing increase in demand for Crysvita in the U.S. and Europe and having a full year of revenue in the U.S. in 2019 as compared to a partial year in 2018. In December 2019, we sold the rights to the royalty payments in the European territory, including the United Kingdom and Switzerland, to Royalty Pharma. Going forward, we will continue to record the royalty revenue in the European territory as non-cash royalties.

Collaboration and license revenue from our research arrangement with Bayer for the year ended December 31, 2019 decreased by $23.0 million compared to the same period in 2018. The decrease was primarily due to the completion of clinical manufacturing and regulatory support activities and transition of the clinical development to Bayer as part of the research arrangement.

Product sales for the year ended December 31, 2019 increased by $10.4 million compared to the same period in 2018. The increase was primarily due to an increase in volume as a result of continued increase in demand for our approved products and certain products under our named patient program in certain countries.

Cost of Sales (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Cost of sales	$ 9,008	$ 1,146	$ 7,862	686%

Cost of sales related to our approved products increased by $7.9 million for the year ended December 31, 2019, compared to the same period in 2018. The increase was due to the commercialization of our approved product Mepsevii, capitalization of manufacturing and related costs which were previously expensed prior to approval, and a reserve on inventory of $5.7 million for the year ended December 31, 2019 for inventory batches that did not meet our quality standards. The cost of sales for the year ended December 31, 2018 included a reserve for excess inventory of $0.4 million. Prior to the approval of our approved products, manufacturing and related costs were expensed; accordingly, these costs were not capitalized and as a result are not fully reflected in the costs of sales during the current period. If manufacturing and related costs were capitalized prior to the approval period, we estimate that cost of sales for the year ended December 31, 2019 and 2018 would have been approximately $9.7 million and $2.1 million, respectively, for our commercial product sales. These estimates include the additional $5.7 million and $0.4 million of reserves on inventory for the year ended December 31, 2019 and 2018, respectively. We expect our gross margin percentage to decrease as we produce Mepsevii at costs that reflect the full costs of manufacturing similar to other biologic products and as we deplete inventories that we had expensed prior to receiving FDA approval.

Research and Development Expenses (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Crysvita	$ 37,872	$ 45,918	$ (8,046)	(18%)
Mepsevii	17,299	24,576	(7,277)	(30%)
UX007	44,695	46,883	(2,188)	(5%)
DTX301	39,191	17,730	21,461	121%
DTX401	33,245	19,304	13,941	72%
DTX201	1,733	26,077	(24,344)	(93%)
GTX102	20,172	—	20,172	100%
Translational Research	57,300	29,410	27,890	95%
Other research costs and preclinical costs	105,848	84,100	21,748	26%
Total research and development expenses	$ 357,355	$ 293,998	$ 63,357	22%

Research and development expenses increased $63.4 million for the year ended December 31, 2019 compared to the same period in 2018. The increase in research and development expenses is primarily due to:

- for Crysvita, a decrease of $8.0 million primarily related to reduced clinical trial activity with the progressive completion of our extension studies and reduced allocation of employees and contractors to R&D support activities, net of KKC reimbursement;
- for Mepsevii, a decrease of $7.3 million primarily related to reduced clinical trial activity with the progressive completion of our extension studies and reduced allocation of employees and contractors to R&D support activities;
- for UX007, a decrease of $2.2 million primarily related to reduced clinical trial expense for the wind-down of the Glut 1 program and reduced manufacturing expense due to the timing of drug substance campaigns, net of increased filing preparation and filing milestone expense for the LC-FAOD program;
- for DTX301, an increase of $21.5 million, primarily related to increases in manufacturing, quality, and clinical activities in support of our Phase 1/2 clinical study;
- for DTX401, an increase of $13.9 million, related to clinical manufacturing, process development expense, and the progressive enrollment of our Phase 1/2 clinical study;
- for DTX201, a decrease of $24.3 million, primarily related to the completion of clinical manufacturing and regulatory support activities for our Bayer collaboration agreement and the corresponding period decrease in intangible asset amortization;
- for GTX102, an increase of $20.2 million, primarily related to the $20.0 million payment in August 2019 for the exclusive option to acquire GeneTx Biotherapeutics LLC;
- for translational research, an increase of $27.9 million primarily related to research, process development, and manufacturing activities, including the progression of our UX701, UX053, and UX068 programs toward IND filings; and
- an increase of $21.7 million in other research and development costs primarily related to the $15.6 million recorded for the consideration attributable to the additional license rights obtained as part of amended Research Collaboration and License Agreement with Arcturus in June 2019 and was recorded as in-process research and development expense, as well as increases in general operating and overhead expenses in support of our clinical and research program pipeline, net of reduced operating expense for terminated programs.

We expect our research and development expenses to continue 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.

Selling, General and Administrative Expenses (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Selling, general and administrative	$ 161,524	$ 127,724	$ 33,800	26%

Selling, general and administrative expenses increased $33.8 million for the year ended December 31, 2019 compared to the same period in 2018. The increase in selling, general and administrative expenses was primarily due to increases in personnel costs resulting from an increase in the number of employees in support of our commercial activities, commercialization costs, and professional services costs.

We expect selling, general and administrative expenses to continue to increase in the future to support our organizational growth and for our expected staged build out of our commercial organization over the next several years related to our approved products and multiple clinical-stage product candidates.

Interest Income (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Interest income	$ 13,238	$ 9,542	$ 3,696	39%

Interest income increased $3.7 million for the year ended December 31, 2019 compared to the same period in 2018, primarily due to an increase in yield of our invested funds during 2019.

Gain from Sale of Priority Review Vouchers (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Gain from sale of priority review vouchers	$ —	$ 170,322	$ (170,322)	(100%)

The gain from the sale of the Priority Review Vouchers, or PRVs, of $170.3 million for the year ended December 31, 2018 was due to the completion of the sales of the PRVs we received from the FDA in connection with the approval of Crysvita and Mepsevii. The Mepsevii PRV was sold in January 2018 for net proceeds of $130.0 million, and the Crysvita PRV was sold in April 2018 for net proceeds of $80.6 million, which was shared equally with KKC.

Change in Fair Value of Investment in Arcturus Equity Securities (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Change in fair value of investment in Arcturus equity securities	$ 13,413	$ —	$ 13,413	100%

The increase in the fair value of our investment in Arcturus equity securities of $13.4 million for the year ended December 31, 2019 was due to the remeasurement to fair value of the Arcturus common stock and option to purchase additional Arcturus stock. Given the historic volatility of the publicly traded stock price of Arcturus, the fair value adjustments of our investments in Arcturus may be subject to wide fluctuations which may have a significant impact on our earnings in future periods.

Non-cash Interest Expense on Liability Related to the Sale of Future Royalties (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Non-cash interest expense on liability related to the sale of future royalties	$ 1,135	$ —	$ 1,135	100%

The non-cash interest expense on liability related to the sale of future royalties of $1.1 million for the year ended December 31, 2019 was due to the interest incurred on the liability related to the sale of future royalties for net sales of Crysvita in the European territory pursuant to the Royalty Purchase agreement entered with RPI in December 2019. To the extent the royalty payments are greater or less than our initial estimates or the timing of such payments is materially different than its original estimates, we will prospectively adjust the effective interest rate.

Other Income (Expense) (dollars in thousands)

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Other income (expense)	$ (787)	$ (5,588)	$ 4,801	(86%)

Other income (expense) decreased $4.8 million for the year ended December 31, 2019 compared to the same period in 2018. The expense recognized during the year ended December 31, 2018 was primarily due to the recognition of cumulative foreign currency translation losses related to the substantial liquidation of subsidiaries with a functional currency other than the U.S. Dollar, which did not recur in 2019.

Benefit from (provision for) income taxes

	Year Ended December 31,		Dollar	%
	2019	2018	Change	Change
Benefit from (provision for) income taxes	$ (3,283)	$ (514)	$ (2,769)	539%

The provision for incomes taxes increased by $2.8 million for the year ended December 31, 2019 compared to the same period in 2018. The increase was primarily due to changes in state tax apportionment which resulted in an increase in the deferred tax liability from the acquisition of Dimension and due to increase in certain foreign taxes as we commercialize our products in foreign territories.

Liquidity and Capital Resources

We have funded our operations primarily from the sale of equity securities and the sale of future royalties.

As of December 31, 2019, we had $760.4 million in available cash, cash equivalents, and investments. We believe that our existing capital resources will be sufficient to fund our projected operating requirements for at least the next twelve months. Our cash, cash equivalents and investments are held in a variety of deposit accounts, interest-bearing accounts, corporate bond securities, U.S government securities and money market funds. 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.

During the year ended December 31, 2019, the proceeds from our at-the-market, or ATM, offering were approximately $24.8 million after commissions and other offering costs. As of December 31, 2019, $20.7 million remained available under our ATM facility. In February 2019, we completed an underwritten public offering in which we sold 5,833,333 shares of common stock and received net proceeds of approximately $330.4 million. In December 2019, we received net proceeds of $314.2 million from the sale of future royalties to RPI.

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

	Year Ended December 31,		
	2019	2018	2017
Cash used in operating activities	$ (345,383)	$ (290,566)	$ (253,843)
Cash provided by (used in) investing activities	(13,039)	(33,331)	55,482
Cash provided by financing activities	679,306	336,853	136,267
Effect of exchange rate changes on cash	(165)	(472)	528
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 320,719	$ 12,484	$ (61,566)

Cash Used in Operating Activities

Our primary use of cash is to fund operating expenses, which consist primarily of research and development and commercial 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, 2019 was $345.4 million and reflected a net loss of $402.7 million, $6.2 million for the amortization of the discount paid on purchased investments, and $13.4 million for a non-cash unrealized gain in the Arcturus equity securities, offset by non-cash charges of $82.0 million for stock-based compensation, $8.5 million for depreciation and amortization, $0.7 million non-cash foreign currency remeasurement losses in connection with fluctuations of exchange rates related to intercompany transactions with foreign subsidiaries that are denominated in our reporting currency, and $1.1 million for non-cash interest incurred on the liability related to the sale of future royalties to Royalty Pharma. Cash used in operating activities also reflected a $20.1 million decrease due to an increase in accounts receivable from the commercialization of Mepsevii and Crysvita, a $4.5 million decrease due to an increase in inventory as we build out our commercial inventory supplies as we commercialize Mepsevii, a $8.2 million decrease due to an increase in prepaid expenses and other assets primarily due to an increase in general receivables, amounts due from a collaboration partner, and amounts owed for a tenant improvement allowance, and a $14.2 million decrease due to the addition of the right-of-use lease assets net of amortization during the period. These decreases were offset by a $13.3 million increase in accounts payable, accrued, and other liabilities primarily due to increased commercial and research activities and the timing of payments and receipt of invoices offset by the derecognition of deferred rent obligations for the new lease accounting guidance, a $15.6 million increase due to the addition of lease liabilities net of amortization during the period, and a $2.1 million increase in deferred tax liabilities due to adjustments made related to the Dimension acquisition.

Cash used in operating activities for the year ended December 31, 2018 was $290.6 million and reflected a net loss of $197.6 million, $170.3 million for the gain from sale of the PRVs, and $2.6 million for the amortization of the discount paid on purchased investments, offset by non-cash charges of $80.1 million for stock-based compensation, $19.5 million for depreciation and amortization, and $5.3 million non-cash foreign currency remeasurement losses in connection with the substantial liquidation of subsidiaries due to a change in the Company's tax structure and fluctuations of exchange rates related to intercompany transactions with foreign subsidiaries that are denominated in our reporting currency. Cash used in operating activities also reflected a $7.6 million decrease due to an increase in accounts receivable from the commercialization of Mepsevii and Crysvita, a $5.3 million decrease due to an increase in inventory as we build out our commercial inventory supplies as we commercialize Mepsevii, and a $14.3 million decrease due to an increase in prepaid expenses and other assets primarily from an increase in prepaid manufacturing costs. These decreases were offset by a $2.4 million increase in accounts payable, accrued, and other liabilities primarily due to increased spend and the timing of payments.

Cash Provided by (Used in) Investing Activities

Cash used in investing activities for the year ended December 31, 2019 was $13.0 million and related to purchases of property and equipment of $24.8 million, purchases of investments of $692.8 million, and purchases of Arcturus equity securities of $14.3 million, offset by proceeds from maturities of investments of $676.2 million and the sale of investments of $42.7 million.

Cash used in investing activities for the year ended December 31, 2018 was $33.3 million and related to purchases of property and equipment of $4.1 million, and purchases of investments of $509.8 million, offset by proceeds from the sale of PRVs of $170.3 million, proceeds from maturities of investments of $302.6 million, and the sale of investments of $7.7 million.

Cash Flows Provided by Financing Activities

Cash provided by financing activities for the year ended December 31, 2019 was $679.3 million and was comprised of $314.2 million related to the sale of future royalties to Royalty Pharma, $330.4 million from the sale of common stock in our underwritten public offering, $24.8 million from the sale of common stock from our ATM offering, and $9.8 million in net proceeds from the issuance of common stock upon the exercise of stock options, offset by taxes withheld from the vesting of restricted stock units.

Cash provided by financing activities for the year ended December 31, 2018 was $336.9 million and was comprised of $271.0 million from the sale of common stock in our underwritten public offering, $38.1 million from the sale of common stock from our ATM offering and $27.8 million in net proceeds from the issuance of common stock upon the exercise of stock options, offset by taxes withheld from the vesting of restricted stock units.

Funding Requirements

We anticipate, excluding non-recurring items, that we will continue to generate annual losses for the foreseeable future as we continue the development of, and seek regulatory approvals for, our product candidates, and continue with commercialization of approved products. We will likely require additional capital to fund our operations, to complete our ongoing and planned clinical studies, to commercialize our products, and to continue investing in early-stage research capabilities to promote our pipeline growth and to further develop our general infrastructure, including building our own Good Manufacturing Practices, or GMP gene therapy manufacturing facility, and such funding may not be available to us on acceptable terms or at all.

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, 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, including the potential development of our own GMP gene therapy manufacturing plant;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing our commercial infrastructure, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, marketing, distribution, acquisition (including whether we exercise our option to acquire GeneTx pursuant to the terms of our Unitholder Option Agreement with them) and other arrangements that we may establish, including any required upfront milestone, royalty, reimbursements or other payments thereunder.

We expect to satisfy future cash needs through existing capital balances and through some combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and other marketing and distribution arrangements. Please see "Risk Factors—Risks Related to Our Financial Condition and Capital Requirements."

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, 2019 (in thousands):

	Payments due by period*				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
Operating leases	$ 10,276	$ 16,544	$ 14,551	$ 7,766	$ 49,137
Manufacturing and service contracts	7,854	461	$ —	$ —	$ 8,315
Total	$ 18,130	$ 17,005	$ 14,551	$ 7,766	$ 57,452

* Includes additional lease payments under an amended lease entered into in January 2020

The terms of certain of our licenses, royalties, development and collaboration agreements, as well as other research and development activities, require us to pay potential future milestone payments based on product development success. The above table excludes such obligations as the amount and timing of such obligations are unknown or uncertain, which potential obligations are further described in Notes 9 and 16 to the accompanying Consolidated Financial Statements.

Recent Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments — Credit Losses, *(Topic 326): Measurement of Credit Losses on Financial Instruments*, which changes the impairment model for most financial assets and certain other instruments. For trade receivables and other instruments, the Company will be required to use a new forward-looking expected loss model that generally will result in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses that are attributable to credit, the losses will be recognized in earnings as allowances. This guidance is effective for the Company on January 1, 2020.

We do not expect for this guidance to have a material impact on our Consolidated Financial Statements and related disclosures.

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*

Equity Risk

We have exposure to equity risk with respect to the equity securities that we hold in Arcturus. The carrying value of our investment in common stock and the option to purchase additional equity securities in Arcturus is $26.1 million and $1.7 million, respectively, as of December 31, 2019. Given the historic volatility of the publicly traded stock price of Arcturus, the fair value of our investments in Arcturus may be subject to wide fluctuations which may have a significant impact on our earnings in future periods.

Interest Rate 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, 2019 and 2018, we had cash, cash equivalents, and investments totaling $760.4 million and $459.7 million, respectively, which include bank deposits, money market funds, U.S. government treasury and agency securities, and investment-grade corporate bond securities 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 100 basis point change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements. To date, we have not experienced a loss of principal on any of our investments.

Foreign Currency Risk

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. For the year ended December 31, 2019, a majority of our revenue and expense activities and capital expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

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

Our financial statements are annexed to this Annual 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 Annual Report, pursuant to Rules 13a-15(b) and 15d-15(b) under 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, 2019. 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 issued by the Committee of Sponsoring Organizations of the Treadway Commission* (2013 framework), 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, 2019 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 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

There have been no 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 quarter ended December 31, 2019, that have materially affected, or are reasonably likely to materially affect our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Ultragenyx Pharmaceutical Inc.:

Opinion on Internal Control over Financial Reporting

We have audited Ultragenyx Pharmaceutical, Inc.'s internal control over financial reporting as of December 31, 2019, 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). In our opinion, Ultragenyx Pharmaceutical Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2019 and related notes and our report dated February 13, 2020 expressed an unqualified opinion thereon.

Basis for Opinion

The Company'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 are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. 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.

Definition and Limitations of Internal Control Over Financial Reporting

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.

/s/ Ernst & Young LLP

San Jose, California
February 13, 2020

Item 9B. Other Information

None.

PART III

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

The information required by this Item is incorporated herein by reference to information in the proxy statement for our 2020 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 relates (the "2020 Proxy Statement"), including under the headings "Proposal No. 1—Election of Class I Directors," "Information About Our Executive Officers," "Corporate Governance—Global Code of Conduct," "Proposal No. 1—Election of Class I Directors—Nomination of Directors," "Board of Directors and Committees," and, as applicable, "Delinquent Section 16(a) Reports." 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, or Code of Ethics. Our Code of Ethics is posted on our corporate governance website located at *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***

The information required by this Item is incorporated herein by reference to information in the 2020 Proxy Statement, including under the headings "Executive Compensation," "Director Compensation," "Board of Directors and Committees—Compensation Committee Interlocks and Insider Participation," "Executive Compensation—Risk Management and Mitigation," and "Executive Compensation—Compensation Committee Report."

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

The information required by this Item is incorporated herein by reference to information in the 2020 Proxy Statement, including under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information."

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

The information required by this Item is incorporated herein by reference to information in the 2020 Proxy Statement, including under the headings "Certain Relationships and Related-Person Transactions," "Corporate Governance," and "Board of Directors and Committees."

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

The information required by this Item is incorporated herein by reference to information in the 2020 Proxy Statement, including under the heading "Proposal No. 2—Ratification of the Selection of Independent Registered Public Accounting Firm."

PART IV

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

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

(1) Consolidated Financial Statements

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

(2) Consolidated Financial Statement Schedules

Consolidated Financial statement schedules have been omitted in this Annual 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

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
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	Description of Common Stock				X
4.4	Warrant, dated as of June 30, 2010, issued to Emil D. Kakkis, M.D., Ph.D.	S-1	11/8/2013	4.3	
4.5	Warrant, dated as of June 14, 2011, issued to Emil D. Kakkis, M.D., Ph.D.	S-1	11/8/2013	4.6	
4.6	Warrant, dated as of June 14, 2011, issued to Emil D. Kakkis, M.D., Ph.D.	S-1	11/8/2013	4.7	
10.1†	Collaboration and License Agreement, dated as of August 29, 2013, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	S-1/A	12/23/2013	10.1	
10.2	Amendment No. 1 to Collaboration and License Agreement, dated as of August 24, 2015, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	11/10/2015	10.2	
10.3	Amendment No. 2 to Collaboration and License Agreement, effective as of November 28, 2016, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.3	
10.4†	Amendment No. 3 to Collaboration and License Agreement, effective September 29, 2017, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.4	
10.5†	Amendment No. 4 to Collaboration and License Agreement, effective as of January 29, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.5	
10.6†	Amendment No. 5 to Collaboration and License Agreement, effective as of April 30, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	8/3/2018	10.1	
10.7*	Amendment No. 6 to Collaboration and License Agreement, effective as of February 1, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	5/7/2019	10.2	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.8*	Amendment No. 7 to Collaboration and License Agreement, effective as of December 5, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	5/7/2019	10.3	
10.9*	Amendment No. 8 to Collaboration and License Agreement, effective as of July 4, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. (formerly, Kyowa Hakko Kirin Co., Ltd.)	10-Q	8/2/2019	10.1	
10.10*	Amendment No. 9 to Collaboration and License Agreement, effective December 23, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd.				X
10.11†	License Agreement, dated as of September 20, 2012, between Ultragenyx Pharmaceutical Inc. and Baylor Research Institute	S-1/A	12/23/2013	10.3	
10.12†	Amendment to the License Agreement, dated as of March 22, 2013, between Ultragenyx Pharmaceutical Inc. and Baylor Research Institute	S-1	11/8/2013	10.4	
10.13†	Exclusive License Agreement, dated as of November 22, 2010, between Ultragenyx Pharmaceutical Inc. and Saint Louis University	S-1/A	12/23/2013	10.8	
10.14	Supply Agreement, dated as of November 19, 2012, between Ultragenyx Pharmaceutical Inc. and CREMER OLEO GmbH & Co KG	10-K	2/21/2018	10.11	
10.15†	License Agreement, dated October 30, 2013, by and between Dimension Therapeutics, Inc. and REGENXBIO Inc. (f/k/a ReGenX Biosciences, LLC), as amended	10-K	2/21/2018	10.13	
10.16†	Option and License Agreement, dated March 10, 2015, by and between Dimension Therapeutics, Inc. and REGENXBIO Inc.	10-K	2/21/2018	10.14	
10.17*	First Amendment to Option and License Agreement, dated March 18, 2019, by and between REGENXBIO, Inc. and Ultragenyx Pharmaceutical Inc. (as assignee of Dimension Therapeutics, Inc.)	10-Q	5/7/2019	10.1	
10.18*	Amended and Restated Collaboration Agreement and License Agreement, dated June 3, 2019, between Ultragenyx Pharmaceutical Inc. and Bayer Healthcare LLC	10-Q	8/2/2019	10.2	
10.19†	Research, Collaboration and License Agreement, dated as of May 5, 2016, by and between Dimension Therapeutics, Inc. and The Trustees of the University of Pennsylvania, as amended	10-K	2/21/2018	10.16	
10.20†	3rd Amendment to Research, Collaboration and License Agreement, entered into as of October 30, 2017, by and between Dimension Therapeutics, Inc. and The Trustees of the University of Pennsylvania	10-K	2/21/2018	10.17	
10.21†	Commercial Supply and Services Agreement – Drug Substance, effective December 7, 2017, between Ultragenyx Europe GmbH and Rentschler Biopharma SE	10-K	2/21/2018	10.18	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.22†	Commercial Supply and Services Agreement – Drug Product, effective January 31, 2018, between Ultragenyx Europe GmbH and Rentschler Biopharma SE	10-K	2/21/2018	10.19	
10.23	Sales Agreement, dated July 27, 2017, between Ultragenyx Pharmaceutical Inc. and Cowen and Company, LLC	10-Q	7/28/2017	1.1	
10.24	Amendment No. 1 to Sales Agreement, dated as of March 30, 2018, between Ultragenyx Pharmaceutical Inc. and Cowen and Company, LLC	8-K	3/30/2018	1.1	
10.25*	Royalty Purchase Agreement, dated as of December 17, 2019, between Ultragenyx Pharmaceutical Inc. and RPI Finance Trust				X
10.26#	2011 Equity Incentive Plan (including forms of Stock Option Grant Notice and Stock Option Agreement thereunder)	S-1	11/8/2013	10.11	
10.27#	Amendment to the 2011 Equity Incentive Plan	S-1	11/8/2013	10.12	
10.28#	2014 Incentive Plan (as amended)	10-K	2/17/2017	10.20	
10.29#	Form of Incentive Stock Option Agreement	S-1/A	1/17/2014	10.14	
10.30#	Form of Non Statutory Stock Option Agreement (Employees)	S-1/A	1/17/2014	10.15	
10.31#	Form of Non Statutory Stock Option Agreement (Employees)(ex-U.S.)	10-Q	5/10/2016	10.3	
10.32#	Form of Non-Statutory Stock Option Agreement (Directors)	S-1/A	1/17/2014	10.16	
10.33#	Form of Restricted Stock Unit Agreement (Employees)	10-Q	5/10/2016	10.1	
10.34#	Form of Restricted Stock Unit Agreement (Employees)(ex-U.S.)	10-Q	5/10/2016	10.2	
10.35#	Form of Restricted Stock Unit Agreement (Directors)	S-1/A	1/17/2014	10.18	
10.36#	Form of Performance Stock Unit Agreement (Current Employees)	10-K	2/21/2018	10.31	
10.37#	Form of Performance Stock Unit Agreement (New Employees)	10-K	2/21/2018	10.32	
10.38#	Form of Performance Stock Unit Agreement (2019)	10-Q	5/7/2019	10.4	
10.39#	2014 Employee Stock Purchase Plan (as amended)	10-K	2/17/2017	10.28	
10.40#	Corporate Bonus Plan	S-1/A	1/17/2014	10.27	
10.41#	Executive Employment Agreement, dated as of June 15, 2011, between Ultragenyx Pharmaceutical Inc. and Emil D. Kakkis, M.D., Ph.D.	S-1	11/8/2013	10.18	
10.42#	Amendment No. 1 to Executive Employment Agreement, dated August 8, 2014, by and between Ultragenyx Pharmaceutical Inc. and Emil D. Kakkis, M.D., Ph.D.	10-Q	8/11/2014	10.2	
10.43#	Offer Letter, dated as of October 31, 2011, between Ultragenyx Pharmaceutical Inc. and Thomas Kassberg	S-1	11/8/2013	10.19	
10.44#	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	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.45#	Offer Letter, dated as of March 12, 2012, between Ultragenyx Pharmaceutical Inc. and Shalini Sharp	S-1	11/8/2013	10.20	
10.46#	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	
10.47#	Offer Letter, dated as of April 26, 2016, between Ultragenyx Pharmaceutical Inc. and Karah Parschauer	10-Q	8/9/2016	10.3	
10.48#	Offer Letter, dated as of February 20, 2015, between Ultragenyx Pharmaceutical Inc. and Dennis Huang	10-K	2/17/2017	10.36	
10.49#	Offer Letter, dated as of June 11, 2015, between Ultragenyx Pharmaceutical Inc. and John R. Pinion II	10-K	2/17/2017	10.37	
10.50#	Offer Letter, dated as of January 15, 2018, between Ultragenyx Pharmaceutical Inc. and Camille Bedrosian, M.D.	10-K	2/21/2018	10.46	
10.51#	Separation Agreement and General Release, dated November 22, 2019, between Ultragenyx Pharmaceutical Inc. and Wladimir Hogenhuis, M.D.	8-K	11/25/2019	10.1	
10.52#	Offer Letter, dated May 16, 2017, by and between Ultragenyx Pharmaceutical Inc. and Erik Harris	10-Q	8/2/2019	10.4	
10.53#	Addendum #1, dated August 8, 2017, to Offer Letter dated May 16, 2017 between Ultragenyx Pharmaceutical Inc. and Erik Harris	10-Q	8/2/2019	10.5	
10.54#	Addendum #2, dated June 19, 2019, to Offer Letter dated May 16, 2017 between Ultragenyx Pharmaceutical Inc. and Erik Harris	10-Q	8/2/2019	10.6	
10.55#	Form of Indemnification Agreement	10-K	3/24/2014	10.23	
10.56	Standard Lease, dated as of July 5, 2011, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	S-1	11/8/2013	10.22	
10.57	Addendum One to Standard Lease, dated as of July 5, 2011, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	10-K	2/26/2016	10.34	
10.58	Addendum Two to Standard Lease, dated as of March 7, 2012, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	10-K	2/26/2016	10.35	
10.59	Addendum #3 to Standard Lease, effective as of February 12, 2014, by and between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	8-K	2/25/2014	10.1	
10.60	Addendum #4 to Standard Lease, effective as of March 9, 2015, by and between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	8-K	3/13/2015	10.1	
10.61	Addendum #5 to Standard Lease, effective as of April 7, 2015, by and between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	10-K	2/26/2016	10.38	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.62	Addendum #6 to Standard Lease, effective as of April 29, 2019, by and between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	10-Q	8/2/2019	10.3	
10.63	Lease Agreement between Marina Boulevard Property, LLC and Ultragenyx Pharmaceutical Inc., dated as of December 8, 2015	10-K	2/26/2016	10.43	
10.64	Indenture of Lease between Dimension Therapeutics, Inc. and Rivertech Associates II, LLC, dated March 11, 2014, as amended	10-K	2/21/2018	10.64	
10.65	Second Lease Amendment to the Lease between Dimension Therapeutics, Inc. and Rivertech Associates II, LLC, dated April 28, 2017	10-K	2/21/2018	10.65	
10.66	Third Lease Amendment to the Lease between Ultragenyx Pharmaceutical Inc. and Rivertech Associates II, LLC, effective December 31, 2018	10-K	2/20/2019	10.66	
10.67	Lease Agreement, by and between Dimension Therapeutics, Inc. and ARE-MA Region No. 20, LLC, dated November 2, 2015, and Consent to Assignment to Ultragenyx Pharmaceutical Inc.	10-K	2/21/2018	10.66	
10.68	First Amendment to Lease Agreement, dated March 20, 2018, between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No. 20, LLC	10-Q	5/8/2018	10.6	
10.69	Second Amendment to Lease Agreement, made July 1, 2018, between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No. 20, LLC	10-Q	8/3/2018	10.3	
10.70	Office Lease, dated April 19, 2019, between Ultragenyx Pharmaceutical Inc. and Woburn MCB II, LLC				X
10.71	Commercial Lease, dated July 2, 2018, between Ultragenyx Pharmaceutical Inc. and 32 Leveroni LLC				X
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 Ultragenyx Pharmaceutical Inc., as required by Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X
31.2	Certification of Chief Financial Officer of Ultragenyx Pharmaceutical Inc., as required by Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
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, formatted in Inline XBRL				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document				X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document				X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				X
104	The cover page from the Company's Annual Report on Form 10-k for the year ended December 31, 2019, formatted in Inline XBRL				

† 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.

* Certain confidential portions of this exhibit were omitted by means of marking such portions with asterisks because the identified confidential portions (i) are not material and (ii) would be competitively harmful if publicly disclosed.

# Indicates management contract or compensatory plan.

§ The certification attached as Exhibit 32.1 that accompanies this Annual Report is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Ultragenyx Pharmaceutical Inc. under the Securities Act or the Exchange Act, whether made before or after the date of this Annual Report, irrespective of any general incorporation language contained in such filing.

Item 16. ***Form 10-K Summary***

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ULTRAGENYX PHARMACEUTICAL INC.

By: /s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer

Date: February 13, 2020

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Emil D. Kakkis, M.D., Ph.D. and Shalini Sharp, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Emil D. Kakkis Emil D. Kakkis, M.D., Ph.D.	President and Chief Executive Officer and Director (Principal Executive Officer)	February 13, 2020
/s/ Shalini Sharp Shalini Sharp	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 13, 2020
/s/ Theodore A. Huizenga Theodore A. Huizenga	Senior Vice President, Corporate Controller (Principal Accounting Officer)	February 13, 2020
/s/ Daniel G. Welch Daniel G. Welch	Chairman of the Board	February 13, 2020
/s/ William Aliski William Aliski	Director	February 13, 2020
/s/ Deborah Dunsire Deborah Dunsire, M.D.	Director	February 13, 2020
/s/ Lars Ekman Lars Ekman, M.D., Ph.D.	Director	February 13, 2020
/s/ Matthew K. Fust Matthew K. Fust	Director	February 13, 2020
/s/ Michael Narachi Michael Narachi	Director	February 13, 2020
/s/ Clay B. Siegall Clay B. Siegall, Ph.D.	Director	February 13, 2020
/s/ Shehnaaz Suliman Shehnaaz Suliman, M.D.	Director	February 13, 2020

Ultragenyx Pharmaceutical Inc.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Ultragenyx Pharmaceutical Inc.:

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Ultragenyx Pharmaceutical Inc. (the "Company") as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019, in conformity with US generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2019, 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 13, 2020 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the US federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Net product sales

Description of the Matter	The Company sells approved products through a limited number of distributors. As discussed in Note 2, when recognizing revenue, the Company makes an estimate of the transaction price, including an assessment of whether to constrain any variable consideration. Product sales are recorded net of estimated government-mandated rebates and chargebacks, estimated product returns, and other deductions at the time revenue is recorded. Limited historical data is available for use in developing such estimates which are periodically reviewed and adjusted as necessary. Auditing the Company's net product sales was complex due to the Company's limited history of product sales and the growth of sales in international markets. The Company's estimates of government mandated rebates, chargebacks and estimated product returns depend on the identification of key customer contract terms and conditions, as well as estimates of sales volumes to different classes of payors. The revenue recognition process can be complex and involves significant judgment to identify and assess the terms and conditions of customer agreements and related government regulations that could affect revenue recognition, as the Company's revenue expands with new customers and new markets.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's process of recording product sales and related rebates, chargebacks and returns. We also tested management's controls related to the identification and assessment of the terms and conditions of customer agreements and the completeness and accuracy of data utilized in the controls, and the calculations supporting management's estimates.

To test net product sales, our audit procedures included, among others, tracing a sample of revenue transactions recognized during the year to source documentation. We also confirmed a sample of outstanding receivable balances directly with the Company's customers. To test management's estimates of rebates, chargebacks and returns, we obtained management's calculations for the respective estimates and performed one or more of the following procedures: developed an independent expectation of the reserve and/or tested management's estimation process to assess whether the recorded reserve balances are within a reasonable range of estimate, agreed relevant inputs to the terms of customer contracts, performed retrospective reviews, performed a sensitivity analysis on the inputs and assumptions used in the estimates and assessed subsequent events, and tested a sample of credits issued throughout the year.

Inventory

Description of the Matter

At December 31, 2019, the Company had inventory of $11.5 million. The Company values inventory at the lower of cost or net realizable value. As discussed in Note 2 of the Company's financial statements, the Company periodically reviews its inventories for excess amounts or obsolescence and writes down or reserves obsolete or otherwise unmarketable inventory to its estimated net realizable value.

Auditing the valuation of the Company's inventories, particularly management's assessment of required reserves for excess inventory, was complex and highly judgmental due to the Company's limited history of product sales. Management determines excess inventory based on expected future demand. Estimates related to future demand are sensitive to significant inputs and assumptions such as acceptance by patients and physicians and the availability of formulary coverage and adequate reimbursement from private third-party payers for the product.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's inventory reserve review process, including management's assessment of the assumptions and data underlying the excess and obsolete inventory valuation.

To test management's estimates of future demand, we performed audit procedures that included, among others, comparing management's projected sales to available historical sales and trend information, and other relevant factors. We also compared on-hand inventories to management's demand forecasts and assessed the projected utilization of the inventory lots including considering any applicable expiration dates. We performed sensitivity analysis of projected sales volumes to evaluate the changes in the inventory reserve that would result from changes in the assumptions. We also tested the clerical accuracy of the Company's model.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2010.

San Jose, California
February 13, 2020

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share amounts)

	December 31,	
	2019	**2018**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 433,584	$ 113,432
Short-term investments	321,646	346,274
Accounts receivable	32,844	12,740
Inventory	11,546	7,065
Prepaid expenses and other current assets	51,397	42,858
Total current assets	851,017	522,369
Property and equipment, net	44,348	20,046
Investment in Arcturus equity securities	27,752	—
Intangible assets, net	129,000	129,223
Goodwill	44,406	44,406
Right-of-use lease assets	30,328	—
Long-term investments	5,174	—
Other assets	3,471	3,514
Total assets	$ 1,135,496	$ 719,558
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 12,871	$ 12,275
Accrued liabilities	83,194	62,450
Short-term lease liabilities	7,235	—
Total current liabilities	103,300	74,725
Deferred tax liabilities	33,306	31,166
Long-term lease liabilities	29,757	—
Liability related to the sale of future royalties	315,369	—
Other liabilities	—	4,759
Total liabilities	481,732	110,650
Commitments and contingencies (Notes 9 and 16)		
Stockholders' equity:		
Preferred stock, par value of $0.001 per share—25,000,000 shares authorized; nil outstanding as of December 31, 2019 and 2018	—	—
Common stock, par value of $0.001 per share—250,000,000 shares authorized; 57,838,220 and 50,860,588 shares issued and outstanding as of December 31, 2019 and 2018, respectively	58	51
Additional paid-in capital	2,086,863	1,639,773
Accumulated other comprehensive loss	(147)	(633)
Accumulated deficit	(1,433,010)	(1,030,283)
Total stockholders' equity	653,764	608,908
Total liabilities and stockholders' equity	$ 1,135,496	$ 719,558

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2019	**2018**	**2017**
Revenues:			
Collaboration and license	$ 83,493	$ 41,693	$ 2,136
Product sales	20,221	9,802	476
Total revenues	103,714	51,495	2,612
Operating expenses:			
Cost of sales	9,008	1,146	1
Research and development	357,355	293,998	231,644
Selling, general and administrative	161,524	127,724	99,909
Total operating expenses	527,887	422,868	331,554
Loss from operations	(424,173)	(371,373)	(328,942)
Interest income	13,238	9,542	4,074
Gain from sale of priority review vouchers	—	170,322	—
Change in fair value of investment in Arcturus equity securities	13,413	—	—
Non-cash interest expense on liability related to the sale of future royalties	(1,135)	—	—
Other income (expense)	(787)	(5,588)	6,530
Loss before income taxes	(399,444)	(197,097)	(318,338)
Benefit from (provision for) income taxes	(3,283)	(514)	16,199
Net loss	$ (402,727)	$ (197,611)	$ (302,139)
Net loss per share, basic and diluted	$ (7.12)	$ (3.97)	$ (7.12)
Shares used in computing net loss per share, basic and diluted	56,576,885	49,775,223	42,453,135

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(In thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Net loss	$ (402,727)	$ (197,611)	$ (302,139)
Other comprehensive income (loss):			
Foreign currency translation adjustments	23	(303)	(10,110)
Transfer of currency translation adjustments balance to other income related to the liquidation of foreign subsidiaries	—	5,272	3,490
Unrealized gain on available-for-sale securities	463	78	35
Other comprehensive income (loss):	486	5,047	(6,585)
Total comprehensive loss	$ (402,241)	$ (192,564)	$ (308,724)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(In thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance as of December 31, 2016	41,240,230	$ 41	$ 1,003,561	$ 905	$ (530,533)	$ 473,974
Issuance of common stock in connection with at-the-market offering, net of issuance costs	2,251,217	2	131,958	—	—	131,960
Fair value of vested stock options assumed from acquisition	—	—	8,979	—	—	8,979
Employee stock-based compensation	—	—	68,014	—	—	68,014
Issuance of common stock under equity plan awards, net of tax	675,624	1	9,250	—	—	9,251
Other comprehensive loss	—	—	—	(6,585)	—	(6,585)
Net loss	—	—	—	—	(302,139)	(302,139)
Balance as of December 31, 2017	44,167,071	44	1,221,762	(5,680)	(832,672)	383,454
Issuance of common stock in connection with underwritten public offering, net of issuance costs	5,043,860	5	270,964	—	—	270,969
Issuance of common stock in connection with at-the-market offering, net of issuance costs	640,257	1	38,055	—	—	38,056
Employee stock-based compensation	—	—	81,165	—	—	81,165
Issuance of common stock under equity plan awards, net of tax	1,009,400	1	27,827	—	—	27,828
Other comprehensive income	—	—	—	5,047	—	5,047
Net loss	—	—	—	—	(197,611)	(197,611)
Balance as of December 31, 2018	50,860,588	51	1,639,773	(633)	(1,030,283)	608,908
Issuance of common stock in connection with underwritten public offering, net of issuance costs	5,833,333	6	330,409	—	—	330,415
Issuance of common stock in connection with at-the-market offering, net of issuance costs	468,685	—	24,828	—	—	24,828
Employee stock-based compensation	—	—	82,025	—	—	82,025
Issuance of common stock under equity plan awards, net of tax	675,614	1	9,828	—	—	9,829
Other comprehensive income	—	—	—	486	—	486
Net loss	—	—	—	—	(402,727)	(402,727)
Balance as of December 31, 2019	57,838,220	$ 58	$ 2,086,863	$ (147)	$ (1,433,010)	$ 653,764

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Operating activities:			
Net loss	$ (402,727)	$ (197,611)	$ (302,139)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	81,995	80,107	68,014
Amortization of premium (discount) on investment securities, net	(6,214)	(2,641)	1,706
Depreciation and amortization	8,539	19,538	5,825
Foreign currency remeasurement (gain) loss	688	5,309	(7,018)
Change in fair value of investment in Arcturus equity securities	(13,413)	—	—
Non-cash interest expense on liability related to the sale of future royalties	1,135	—	—
Gain from sale of priority review vouchers	—	(170,322)	—
Other	557	(156)	—
Changes in operating assets and liabilities:			
Accounts receivable	(20,104)	(7,583)	(5,172)
Inventory	(4,451)	(5,283)	(757)
Prepaid expenses and other assets	(8,216)	(14,285)	3,113
Right-of-use lease assets	(14,176)	—	—
Accounts payable, accrued, and other liabilities	13,312	2,361	(1,169)
Lease liabilities	15,552	—	—
Deferred tax liabilities	2,140	—	(16,246)
Net cash used in operating activities	(345,383)	(290,566)	(253,843)
Investing activities:			
Purchase of property and equipment	(24,832)	(4,076)	(2,793)
Purchase of investments	(692,824)	(509,796)	(230,487)
Purchase of investment in Arcturus equity securities	(14,339)	—	—
Proceeds from sale of investments	42,718	7,655	157,934
Proceeds from maturities of investments	676,238	302,564	273,632
Proceeds from sale of priority review vouchers	—	170,322	—
Acquisition, net of cash acquired	—	—	(142,804)
Net cash provided by (used in) investing activities	(13,039)	(33,331)	55,482
Financing activities:			
Proceeds from the sale of future royalties, net	314,234	—	—
Proceeds from the issuance of common stock in connection with underwritten public offerings, net	330,415	270,969	—
Proceeds from the issuance of common stock in connection with at-the-market offering, net	24,828	38,056	131,960
Proceeds from the issuance of common stock under equity plan awards, net	9,829	27,828	9,251
Repayment of note payable	—	—	(4,944)
Net cash provided by financing activities	679,306	336,853	136,267
Effect of exchange rate changes on cash	(165)	(472)	528
Net increase (decrease) in cash, cash equivalents, and restricted cash	320,719	12,484	(61,566)
Cash, cash equivalents, and restricted cash at beginning of year	115,525	103,041	164,607
Cash, cash equivalents, and restricted cash at end of year	$ 436,244	$ 115,525	$ 103,041
Supplemental disclosures of non-cash investing and financing information:			
Acquired lease liabilities arising from obtaining right-of-use lease assets	$ 21,861	$ —	$ —
Stock-based compensation capitalized into ending inventory	$ 1,206	$ 1,058	$ —
Costs of property and equipment included in accounts payable and other liabilities	$ 10,367	$ 1,192	$ 400
Fair value of vested stock options assumed in acquisition	$ —	$ —	$ 8,979

See accompanying notes.

1. Organization and Basis of Presentation

Ultragenyx Pharmaceutical Inc. (the Company) is a biopharmaceutical company 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 serious rare and ultra-rare genetic diseases. The Company has two approved therapies. Crysvita® (burosumab) is approved in the United States by the U.S. Food and Drug Administration (FDA) and in Canada for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients one year of age and older, and has received European conditional marketing authorization for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing skeletons. In Brazil, Crysvita is approved for treatment of XLH in adult and pediatric patients one year of age and older. The Company has also received FDA approval for Mepsevii™ (vestronidase alfa), the first medicine approved for the treatment of children and adults with mucopolysaccharidosis VII (MPS VII), also known as Sly syndrome. In the European Union and the United Kingdom, Mepsevii is approved under exceptional circumstances for patients of all ages for the treatment of non-neurological manifestations of MPS VII. In Brazil, Mepsevii is approved for the treatment of MPS VII for patients of all ages.

In addition to the approved treatments for XLH and MPS VII, the Company has four ongoing clinical development programs. Crysvita is being studied for the treatment of tumor induced osteomalacia (TIO), a rare disease that impairs bone mineralization. UX007 is being studied 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. The Company has two gene therapy pipeline candidates: DTX301 is an adeno-associated virus 8 (AAV8) gene therapy product candidate in development for the treatment of patients with ornithine transcarbamylase (OTC) deficiency, the most common urea cycle disorder; and DTX401 is an AAV8 gene therapy product candidate for the treatment of patients with glycogen storage disease type Ia (GSDIa). The Company operates as one reportable segment.

The Company has sustained operating losses and expects such annual losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development and commercialization activities, for which it expects to incur additional losses in the future. Management recognizes the need to raise additional capital to fully implement its business plan. Through December 31, 2019, the Company has relied primarily on the proceeds from equity offerings and its sale of future royalties to finance its operations.

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 wholly-owned 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, 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, Cash Equivalents, and Restricted Cash

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.

Restricted cash primarily consists of money market accounts used as collateral for the Company's obligations under its facility leases.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the amounts shown in the consolidated statement of cash flows (in thousands):

	December 31,		
	2019	2018	2017
Cash and cash equivalents	$ 433,584	$ 113,432	$ 100,488
Restricted cash included in prepaid expenses and other current assets	161	271	461
Restricted cash included in other assets	2,499	1,822	2,092
Total cash, cash equivalents, and restricted cash shown in the statements of cash flows	$ 436,244	$ 115,525	$ 103,041

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 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 other income (expense). The cost of securities sold is based on the specific-identification method. Interest on investments is included in interest income.

Investment in Equity Securities

In June 2019, the Company entered into an amendment to the Research Collaboration and License Agreement and an Equity Purchase Agreement with Arcturus Therapeutics Holdings Inc. (Arcturus). Pursuant to the Equity Purchase Agreement, the Company purchased 2,400,000 shares of common stock, or approximately 18.2% of Arcturus’s outstanding shares of common stock as of the closing date of the transaction and received an option to purchase an additional 600,000 shares of common stock. The investment is subject to the equity method of accounting as it was determined that the Company has significant influence over Arcturus, but does not control the significant activities of Arcturus. The Company elected to apply the fair value option to account for the equity investment in Arcturus. The decision to elect the fair value option is irrevocable and is determined on an instrument by instrument basis. The option to purchase additional stock is accounted for at fair value using the Black-Scholes option pricing method. The changes in fair value of the equity investment and option to purchase additional stock are included in the Consolidated Statements of Operations. See “Note 8. License and Research Agreements” for additional details on the Arcturus transaction.

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, commercial paper, 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 issuers, and other financial instruments, to the extent recorded in the balance sheets.

The Company has not experienced any credit losses to date from credit risk concentration. Concentration of credit risk with respect to accounts receivable from customers is primarily limited to collaboration partners, drug wholesalers, and retail pharmacy distributors. Credit is extended to our customers based on an evaluation of a customer’s financial condition, and collateral is not required. Further, the Company maintains a policy to record allowances for potentially doubtful accounts for estimated losses resulting from the inability of customers to make required payments. As of December 31, 2019, there were no allowances for doubtful accounts and the Company has not had any write-offs historically.

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

Inventory

The Company values inventory at the lower of cost and net realizable value and determines the cost of inventory using the average-cost method. The Company expenses costs associated with the manufacture of product candidates prior to regulatory approval. Inventories consist of currently approved products. The Company periodically reviews its inventories for excess amounts or

obsolescence and writes down obsolete or otherwise unmarketable inventory to its estimated net realizable value. Management determines excess inventory based on expected future demand. Estimates related to future demand are sensitive to significant inputs and assumptions such as acceptance by patients and physicians and the availability of formulary coverage and adequate reimbursement from private third-party payers for the product.

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 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

Intangible Assets

The Company recognizes an acquired intangible apart from goodwill whenever the intangible arises from contractual or other legal rights, or whenever it can be separated or divided from the acquired entity and sold, transferred, licensed, rented or exchanged, either individually or in combination with a related contract, asset or liability. The Company's intangible assets consist of acquired in-process research and development (IPR&D) and an acquired contract asset.

IPR&D assets represent capitalized incomplete research projects that the Company acquired through business combinations. Such assets are initially measured at their acquisition date fair values and are tested for impairment, until the completion or abandonment of the associated research and development efforts. If and when development is complete, which generally occurs when regulatory approval to market a product is obtained, the associated assets will be deemed finite-lived and will be amortized over a period that best reflects the economic benefits provided by these assets. The acquired contract asset was initially recorded at fair value and is amortized over its estimated useful life.

The Company tests its definite and indefinite-lived intangible assets for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired. If it is determined that the asset becomes impaired, the carrying value is written down to its fair value with the related impairment charge recognized in consolidated statements of operations in the period in which the impairment occurs. The Company has not recorded any impairments of intangible assets.

Goodwill

Goodwill represents the excess of purchase price over fair value of net assets acquired in a business combination and is not amortized. Goodwill is subject to impairment testing at least annually during the fourth quarter or when a triggering event occurs that could indicate a potential impairment. If it is determined that the goodwill becomes impaired, the carrying value is written down to its fair value with the related impairment charge recognized in consolidated statements of operations in the period in which the impairment occurs. The Company has not recorded any impairments of goodwill.

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.

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.

Revenue Recognition

Collaboration and license revenue

The Company has certain license and collaboration agreements that are within the scope of Accounting Standards Codification (ASC) 808, *Collaborative Agreements*, which provides guidance on the presentation and disclosure of collaborative arrangements. Generally, the classification of the transactions under the collaborative arrangements is determined based on the nature of contractual terms of the arrangement, along with the nature of the operations of the participants. When the collaborative partner is the principal in the sale transaction with the customer, the Company records its share of collaboration profit as collaboration revenue. Funding received related to research and development services and commercialization costs is generally classified as a reduction of research and development expenses and selling, general and administrative expenses, respectively, in the consolidated statement of operations, because the provision of such services for collaborative partners are not considered to be part of the Company's ongoing major or central operations.

The Company also receives royalty revenues under certain of the Company's license or collaboration agreements in exchange for license of intellectual property. If the Company does not have any future performance obligations for these license or collaboration agreements, royalty revenue is recorded as the underlying sales occur.

In order to record collaboration revenue, the Company utilizes certain information from its collaboration partners, including revenue from the sale of the product, associated reserves on revenue, and costs incurred for development and sales activities. For the periods covered in the financial statements presented, there have been no material changes to prior period estimates of revenues and expenses.

The terms of the Company's collaboration agreements may contain multiple performance obligations, which may include licenses and research and development activities. The Company evaluates these agreements under ASC 606, *Revenue from Contracts with Customers* (ASC 606), to determine the distinct performance obligations. The Company analogizes to ASC 606 for the accounting for distinct performance obligations for which there is a customer relationship. Prior to recognizing revenue, the Company makes estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Total consideration may include nonrefundable upfront license fees, payments for research and development activities, reimbursement of certain third-party costs, payments based upon the achievement of specified milestones, and royalty payments based on product sales derived from the collaboration.

If there are multiple distinct performance obligations, the Company allocates the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost plus margin. The Company estimates the efforts needed to complete the performance obligation and recognizes revenue by measuring the progress towards complete satisfaction of the performance obligation using an input measure.

Product sales

The Company sells its approved products through a limited number of distributors. Under ASC 606, revenue from product sales is recognized at the point in time when the delivery is made and when title and risk of loss transfers to these distributors. The Company also recognizes revenue from sales of certain products on a "named patient" basis, which are allowed in certain countries prior to the commercial approval of the product. Prior to recognizing revenue, the Company makes estimates of the transaction price, including any variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Product sales are recorded net of estimated government-mandated rebates and chargebacks, estimated product returns, and other deductions.

Provisions for returns and other adjustments are provided for in the period the related revenue is recorded, as estimated by management. These reserves are based on estimates of the amounts earned or to be claimed on the related sales and are reviewed

periodically and adjusted as necessary. If actual results vary, the Company may need to adjust these estimates, which could have an effect on earnings in the period of the adjustment.

Leases

The Company adopted Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)* as of January 1, 2019 using the modified retrospective method. The results for year ended December 31, 2019 are presented under ASC 842. The results for the year ended December 31, 2018 and other prior period amounts were not adjusted and continue to be reported in accordance with historical accounting under prior lease guidance, ASC 840, *Leases (Topic 840)*. The Company also elected the package of practical expedients under the transition guidance that will retain the historical lease classification and initial direct costs for any leases that existed prior to adoption of the new guidance and the practical expedient to not separate lease and non-lease components.

The Company determines if an arrangement includes a lease at inception. Right-of-use lease assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. The right-of-use lease asset includes any lease payments made and excludes lease incentives. Incremental borrowing rate is used in determining the present value of future payments. The Company applies a portfolio approach to the property leases to apply an incremental borrowing rate to leases with similar lease terms. The lease terms may include options to extend or terminate the lease. The Company recognizes the options to extend the lease as part of the right-of-use lease assets and lease liabilities only if it is reasonably certain that the option would be exercised. Lease expense for minimum lease payments is recognized on a straight-line basis over the non-cancelable lease term.

As a result of the adoption of the new guidance, the Company recorded a right-of-use lease asset of $16.2 million, a short-term lease liability of $4.5 million, and a long-term lease liability of $17.0 million and no cumulative effect adjustment was made to the retained earnings as of the adoption date. In addition, as of the adoption date, the Company derecognized a net deferred rent obligation of $5.2 million. See “Note 9. Leases” for further disclosure.

Comprehensive Loss

Comprehensive loss is the change in stockholders’ equity 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 and foreign currency translation adjustments.

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. The deferred 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, restricted stock units (RSUs), and performance stock units (PSUs) are recorded at fair value as of the grant date and recognized as expense on a straight-line basis over the employee’s requisite service period (generally the vesting period). PSUs vest only if certain specified criteria are achieved and the employees’ continued service requirements are met; therefore, the expense recognition occurs when the likelihood of the PSUs being earned is deemed probable. Stock compensation expense on awards expected to vest are recognized net of estimated forfeitures.

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.

In conjunction with Dimension acquisition, a deferred tax liability was recorded reflecting the tax impact of the difference between the book basis and tax basis of acquired IPR&D. Such deferred income tax liability is not used to offset deferred tax assets when analyzing the Company’s valuation allowance as the acquired IPR&D is considered to have an indefinite life until the Company completes or abandons development of the acquired IPR&D.

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.

Foreign Currency

Assets and liabilities of non-U.S. subsidiaries that operate in a local currency environment, where the local currency is the functional currency, are translated to U.S. dollars at exchange rates in effect at the balance sheet date, with the resulting translation adjustments directly recorded to a separate component of accumulated other comprehensive loss. Income and expense accounts are translated at average exchange rates for the period. Transactions which are not in the functional currency of the entity are remeasured into the functional currency and gains or losses resulting from the remeasurement recorded in other income (expense).

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive. In periods when we have incurred a net loss, options and warrants to purchase common stock are considered common stock equivalents, but have been excluded from the calculation of diluted net loss per share, as their effect is antidilutive.

Business Combinations

The Company applies the provisions of ASC 805, *"Business Combinations"*, in the accounting for acquisitions. The Company allocates the purchase price of acquired businesses to the tangible and intangible assets acquired and liabilities assumed based upon their estimated fair values on the acquisition date. The purchase price allocation process requires management to make significant estimates and assumptions, especially at the acquisition date with respect to intangible assets which includes IPR&D.

Recent Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments — Credit Losses, *(Topic 326): Measurement of Credit Losses on Financial Instruments*, which changes the impairment model for most financial assets and certain other instruments. For trade receivables and other instruments, the Company will be required to use a new forward-looking expected loss model that generally will result in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses that are attributable to credit, the losses will be recognized in earnings as allowances. This guidance is effective for the Company on January 1, 2020, and early adoption is permitted. The Company does not expect that this guidance will have a material impact on its Consolidated Financial Statements and related disclosures.

3. Dimension Acquisition

On November 7, 2017, the Company acquired all of the issued and outstanding share capital of Dimension Therapeutics, Inc. (Dimension), headquartered in Cambridge, Massachusetts for a purchase price of $6.00 per share or $152.3 million in cash. In connection with the acquisition, the Company also paid a $2.9 million termination fee to REGENXBIO Inc. (REGENX), as a result of a previously existing merger agreement between REGENX and Dimension and assumed all the outstanding equity awards of Dimension at the date of the acquisition. The assumed equity awards were valued at $15.4 million using a Black-Scholes option pricing model on the acquisition date. The equity awards assumed were allocated as follows: $9.0 million to the purchase consideration relating to the vested portion of stock options assumed, $2.2 million for the acceleration of certain awards that were recognized immediately as expense in the post-combination financial statements, and $4.2 million is being recognized as expense after the acquisition date over the employee's remaining service period. The acquisition date fair value of the consideration transferred for Dimension was approximately $164.1 million, which consisted of the following (in thousands):

Cash payments	$	152,292
Fair value of vested stock options assumed		8,979
REGENX termination fee		2,850
Fair value of total consideration	$	164,121

The following table summarizes the fair values of assets acquired and liabilities assumed as of the date of acquisition (in thousands):

Cash and cash equivalents	$	12,338
Short-term investments		9,737
Other current assets		11,155
Property and equipment		6,580
In-process research and development		129,000
Bayer collaboration agreement		13,526
Accounts payable and accrued liabilities		(10,265)
Notes payable		(4,944)
Deferred tax liabilities		(47,412)
Net identifiable net assets acquired		119,715
Goodwill		44,406
Net assets acquired	$	164,121

The transaction was accounted for as a business combination under the acquisition method of accounting as outlined in ASC 805, *Business Combinations*. The excess of purchase consideration over the fair value of net tangible and identifiable intangible assets acquired was recorded as goodwill. The fair values assigned to tangible and identifiable intangible assets acquired and liabilities assumed were based on management's estimates and assumptions based on the information that was available as of the date of the acquisition. See also "Note 6. Intangible Assets, net" for a description of the intangible assets.

The Company recorded $47.4 million in non-current deferred tax liability resulting from the acquisition reflecting the tax impact of the difference between the book basis and tax basis of acquired IPR&D. Such deferred income tax liability is not used to offset deferred tax assets when analyzing the Company's valuation allowance as the acquired IPR&D is considered to have an indefinite life until the Company completes or abandons development of the acquired IPR&D. Subsequent to the acquisition date, the deferred tax liability was reduced to $31.2 million due to the reduction of U.S. corporate tax rate from 34% to 21% in December 2017. As of December 31, 2019, the deferred tax liability was increased to $33.3 million due to changes in the estimated state tax apportionment.

The goodwill balance is primarily attributed to the deferred tax liabilities arising from the temporary differences on IPR&D assets between book and tax basis as well as the relating to the assembled workforce and expanded market opportunities when integrating Dimension's research with the Company. The goodwill balance is not deductible for U.S. income tax purposes.

The assumed notes payable of $4.9 million, along with the outstanding interest was repaid in December 2017. In connection with the acquisition, the Company recognized transaction costs of $6.0 million as selling, general and administrative expense.

There were no purchase price adjustments subsequent to the acquisition.

Pro Forma Financial Information

The Company's consolidated statement of operations from November 7, 2017 through December 31, 2017 includes Dimension total revenue of $2.1 million and a net loss of $7.5 million. If the acquisition had occurred on January 1, 2017, the supplemental unaudited pro forma financial results is $18.5 million in total revenues and $341.7 million in net loss for the year ended December 31, 2017.

The unaudited pro forma financial information include pro forma adjustments that assume the acquisition occurred on January 1, 2017. These items include adjustments to remove the impact of transaction costs related to the acquisition of $9.6 million for the year ended December 31, 2017 and to record the amortization of definite-lived intangible assets of $1.8 million for the year ended December 31, 2017. Other adjustments include reduction of interest income, amounts related to severance of certain employees, acceleration of certain equity awards, and adjustments to conform to the Company's accounting policies on revenue. These unaudited pro forma results are presented for informational purposes only and are not necessarily indicative of what the actual results of operations of the combined company would have been if the acquisition had occurred at the beginning of the period presented, nor are they indicative of future results of operations.

4. 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 receivable, 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, Level 2, and Level 3 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.

The Company determines the fair value of the Arcturus common stock by using the quoted market price on December 31, 2019, which is a Level 1 fair value measurement. The change in fair value of the Arcturus common stock for the year ended December 31, 2019 was $12.2 million, which was recognized in the Consolidated Statements of Operations.

The fair value of the option to purchase additional shares of Arcturus common stock was based on unobservable inputs that are significant to the measurement of the fair value of the asset and is supported by little or no market data; accordingly, the fair value of the option is considered a Level 3 financial asset. The Company measures the Level 3 financial asset by applying the Black-Scholes option pricing method and utilizes the following inputs: stock price, strike price, volatility, risk free interest rate, and expected term. The expected term is the Company's estimated period to purchase additional stock. The change in fair value of the option to purchase additional Arcturus common stock for the year ended December 31, 2019 was $1.2 million, which was recognized in the Consolidated Statements of Operations.

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, 2019			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 293,309	$ —	$ —	$ 293,309
Repurchase agreements	—	100,000	—	100,000
Time deposits	—	10,000	—	10,000
Corporate bonds	—	77,026	—	77,026
Commercial paper	—	80,119	—	80,119
Asset-backed securities	—	30,406	—	30,406
U.S. Government Treasury and agency securities	96,329	53,979	—	150,308
Investment in Arcturus equity securities	26,088	—	1,664	27,752
Total	$ 415,726	$ 351,530	$ 1,664	$ 768,920

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 48,999	$ —	$ —	$ 48,999
Repurchase agreements	—	24,000	—	24,000
Time deposits	—	10,000	—	10,000
Corporate bonds	—	179,926	—	179,926
Commercial paper	—	50,198	—	50,198
Asset-backed securities	—	22,587	—	22,587
U.S. Government Treasury and agency securities	—	99,034	—	99,034
Total	$ 48,999	$ 385,745	$ —	$ 434,744

5. Balance Sheet Components

Cash Equivalents and Investments

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

	December 31, 2019			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds	$ 293,309	$ —	$ —	$ 293,309
Repurchase agreements	100,000	—	—	100,000
Time deposits	10,000	—	—	10,000
Corporate bonds	77,022	17	(13)	77,026
Commercial paper	80,119	—	—	80,119
Asset-backed securities	30,375	31	—	30,406
U.S. Government Treasury and agency securities	150,184	124	—	150,308
Total	$ 741,009	$ 172	$ (13)	$ 741,168

	December 31, 2018			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds	$ 48,999	$ —	$ —	$ 48,999
Repurchase agreements	24,000	—	—	24,000
Time deposits	10,000	—	—	10,000
Corporate bonds	180,167	—	(241)	179,926
Commercial paper	50,198	—	—	50,198
Asset-backed securities	22,597	—	(10)	22,587
U.S. Government Treasury and agency securities	99,087	2	(55)	99,034
Total	$ 435,048	$ 2	$ (306)	$ 434,744

At December 31, 2019, the remaining contractual maturities of available-for-sale securities were less than two years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented. All marketable securities with unrealized losses at December 31, 2019 have been in a loss position for less than twelve months or the loss is not material and were temporary in nature. We do not intend to sell the investments that are in an unrealized loss position before recovery of their amortized cost basis.

Inventory

Inventory consists of the following (in thousands):

	December 31,	
	2019	2018
Work-in-process	$ 8,191	$ 5,384
Finished goods	3,355	1,681
Total	$ 11,546	$ 7,065

Property and Equipment, net

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

	December 31,	
	2019	2018
Leasehold improvements	$ 16,871	$ 15,705
Research and development equipment	17,881	9,856
Furniture and office equipment	3,496	3,379
Computer equipment and software	7,817	7,342
Construction-in-progress	24,271	1,970
Property and equipment, gross	70,336	38,252
Less accumulated depreciation	(25,988)	(18,206)
Property and equipment, net	$ 44,348	$ 20,046

Depreciation expense for the years ended December 31, 2019, 2018 and 2017 was $8.3 million, $7.2 million and $4.8 million respectively. Amortization of leasehold improvements and software is included in depreciation expense.

Accrued Liabilities

Accrued liabilities consists of the following (in thousands):

	December 31,	
	2019	2018
Research, clinical study, and manufacturing expenses	$ 22,894	$ 16,912
Payroll and related expenses	41,324	36,443
Other	18,976	9,095
Total	$ 83,194	$ 62,450

6. Intangible Assets, net

In connection with the acquisition as described in Note 3 “Dimension Acquisition" the Company recognized IPR&D assets of $129.0 million and a contract asset of $13.5 million. The estimated fair value of these intangible assets was measured using Level 3 inputs as of the acquisition date.

IPR&D assets represent the fair value of acquired programs to develop an AAV gene therapy for OTC deficiency and to develop an AAV gene therapy for glycogen storage disease type Ia. The fair value of IPR&D assets acquired was determined based on the discounted present value of each research project’s projected cash flows using an income approach, including the application of probability factors related to the likelihood of success of the program reaching final development and commercialization. Additionally, the projections consider the relevant market sizes and growth factors, estimated future cash flows from product sales resulting from completed products and in-process projects and timing and costs to complete the in-process projects. The rates utilized to discount the net cash flows to their present value are commensurate with the stage of development of the projects and uncertainties in the economic estimates used in the projections. IPR&D assets are considered to be indefinite-life until the completion or abandonment of the associated research and development efforts.

The contract asset represents the fair value of the agreement with Bayer HealthCare LLC to research, develop, and commercialize AAV gene therapy products for treatment of hemophilia A. The fair value of the contract asset was determined based on the discounted present value of the estimated net future income and was amortized to research and development expense over the research term which was completed in 2019. The Company recorded research and development expense of $0.2 million, $12.3 million, and $1.0 million for the years ended December 31, 2019, 2018, and 2017, respectively, related to the amortization of the asset.

The Company tests the intangible assets for impairment annually during its fourth quarter. No impairment charges have been recognized on intangible assets.

7. Revenue

The following table disaggregates total revenues from external customers by collaboration and license revenue and product sales (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Collaboration and license revenue:			
KKC (Crysvita)	$ 82,989	$ 18,226	$ 9
Bayer	504	23,467	2,127
Total collaboration and license revenue	83,493	41,693	2,136
Product sales:			
Crysvita	4,286	644	—
Mepsevii	12,634	7,903	476
UX007	3,301	1,255	—
Total product sales	20,221	9,802	476
Total revenues	$ 103,714	$ 51,495	$ 2,612

The following table disaggregates total revenues based on geographic location (in thousands):

	Year Ended December 31,		
	2019	2018	2017
United States	$ 86,442	$ 45,339	$ 2,289
Europe	12,085	5,293	323
All other	5,187	863	—
Total revenues	$ 103,714	$ 51,495	$ 2,612

The following table presents the activity and ending balances for sales-related accruals and allowances (in thousands):

	December 31,		
	2019	2018	2017
Balance of product sales reserve at beginning of year	$ 1,240	$ 41	$ —
Provisions	3,846	2,466	41
Payments and adjustments	(3,268)	(1,267)	—
Balance of product sales reserve at end of year	$ 1,818	$ 1,240	$ 41

The following table presents changes in the contract assets (liabilities) for the years ended December 31, 2019 and 2018 (in thousands):

	December 31,	
	2019	2018
Balance of contract assets (liabilities) at beginning of year	$ 2,979	$ (5,986)
Additions	504	24,055
Deductions	(3,483)	(15,090)
Balance of contract assets at end of year	$ —	$ 2,979

The Company's largest accounts receivable balance was from a collaboration partner and was 87% and 88% of the total accounts receivable balance as of December 31, 2019 and 2018, respectively.

8. License and Research Agreements

Kyowa Kirin Co., Ltd. Collaboration and License Agreement

In August 2013, the Company entered into a collaboration and license agreement with Kyowa Kirin Co., Ltd. (KKC or formerly Kyowa Hakko Kirin Co., Ltd. or KHK). Under the terms of this collaboration and license agreement, as amended, the Company and KKC collaborate on the development and commercialization of Crysvita in the field of orphan diseases in the United States and Canada, or the profit-share territory, and in the European Union, United Kingdom, and Switzerland, or the European territory, and the Company has the right to develop and commercialize such products in the field of orphan diseases in Mexico and Central and South America, or Latin America.

Development Activities

In the field of orphan diseases, and except for ongoing studies being conducted by KKC, the Company is the lead party for development activities in the profit-share territory and in the European territory until the applicable transition date; the Company is also the lead party for core development activities conducted in Japan and Korea, for which the core development plan is limited to clinical trials mutually agreed to by the Company and KKC. The Company shares the costs for development activities in the profit-share territory and the European territory conducted pursuant to the development plan before the applicable transition date equally with KKC. KKC is responsible for 100% of the costs for development activities in Japan and Korea. In April 2023, which is the transition date for the profit-share territory, and on the applicable transition date for the European territory, KKC 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 KKC. Crysvita was approved in the European Union and United Kingdom in February 2018 and was approved by the FDA in April 2018.

The collaboration and license agreements are within the scope of ASC 808, which provides guidance on the presentation and disclosure of collaborative arrangements.

Collaboration revenue related to sales in profit-share territory

The Company and KKC share commercial responsibilities and profits in the profit-share territory until April 2023. Under the collaboration agreement, KKC manufactures and supplies Crysvita for commercial use in the profit-share territory and charges the Company the transfer price of 35% of net sales through December 31, 2022, and 30% thereafter. The remaining profit or loss after supply costs from commercializing products in the profit-share territory are shared between the Company and KKC on a 50/50 basis until April 2023. Thereafter, the Company will be entitled to receive a tiered double-digit revenue share in the mid-to-high 20% range.

As KKC is the principal in the sale transaction with the customer, the Company recognizes a pro-rata share of collaboration revenue, net of transfer pricing, in the period the sale occurs. The Company concluded that its portion of KKC's sales in the profit-share territory is analogous to a royalty and therefore recorded its share as collaboration revenue, similar to a royalty.

Royalty revenue related to sales in European territory

KKC has the commercial responsibility for Crysvita in the European territory. Prior to the Company's sale of the royalty to Royalty Pharma, as described below, the Company received a royalty of up to 10% on net sales in the European territory, which was recognized as the underlying sales occur.

The Company's share of collaboration and royalty revenue related to Crysvita was as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Company's share of collaboration revenue in profit-share territory	$ 74,869	$ 15,334	$ —
Royalty revenue in European territory	8,120	2,892	9
Total	$ 82,989	$ 18,226	$ 9

In December 2019, the Company entered into a Royalty Purchase Agreement with RPI Finance Trust (RPI), an affiliate of Royalty Pharma, and sold the future royalty payments related to Crysvita sales in the European territory to RPI. Going forward, the Company will record the royalty revenue in European territory as non-cash royalties. See "Note 11. Liability Related to the Sale of Future Royalties".

Product revenue related to sales in other territories

The Company is responsible for commercializing Crysvita in Latin America and Turkey. The Company is considered the principal in these territories as the Company controls the product before it is transferred to the customer. Accordingly, the Company records revenue on a gross basis related to the sale of Crysvita once the product is delivered and the risk and title of the product is transferred to the distributor. For the years ended December 31, 2019 and 2018, the Company recorded product sales of $4.3 million and $0.6 million, respectively, net of estimated product returns and other deductions. There were no product sales recorded for Crysvita for the year ended December 31, 2017. KKC has the option to assume responsibility for commercialization efforts in Turkey from the Company, after a certain minimum period.

Under the collaboration agreement, KKC manufactures and supplies Crysvita, which is purchased by the Company for sales in the above territories, and is based on 35% of the net sales through December 31, 2022 and 30% thereafter. The Company also pays to KKC a low single-digit royalty on net sales in Latin America.

Cost sharing payments

Under the collaboration agreement, KKC and the Company share certain development and commercialization costs. As a result, the Company was reimbursed for these costs and operating expenses were reduced as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Research and development	$ 27,309	$ 32,240	$ 31,165
Selling, general and administrative	21,828	14,228	4,466
Total	$ 49,137	$ 46,468	$ 35,631

Collaboration receivable and payable

The Company had accounts receivable from KKC in the amount of $28.5 million and $11.2 million from profit-share revenue and royalties and other receivables recorded in prepaid and other current assets of $17.8 million and $11.1 million and accrued liabilities of $0.9 million and $0.3 million from commercial and development activity reimbursements, as of December 31, 2019 and 2018, respectively.

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 made a milestone payment of $0.1 million upon approval of Mepsevii for treatment of MPS 7. The Company is required to pay to SLU a low single-digit royalty on net sales of the licensed products in any country or region, upon reaching a certain level of cumulative worldwide sales of the product.

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 its territories for certain intellectual property related to triheptanoin (UX007).

The Company may be obligated to make future payments of up to $5.3 million contingent upon attainment of various development milestones relating to the development of LC-FAOD 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.

REGENXBIO, Inc.

The Company has a license agreement with REGENX, for an exclusive, sublicensable, worldwide commercial license under certain intellectual property for preclinical and clinical research and development, and commercialization of drug therapies using REGENX 's licensed patents for the treatment of hemophilia A, OTC deficiency, and GSD1a. The Company will pay an annual fee and certain milestone fees per disease indication, low to mid single-digit royalty percentages on net sales of licensed products, and milestone and sublicense fees owed by REGENX to its licensors, contingent upon the attainment of certain development activities as outlined in the agreement.

The Company also has an option and license agreement with REGENX under which the Company has an exclusive, sublicensable, worldwide license to make, have made, use, import, sell, and offer for sale licensed products with respect to three disease indications, subject to certain exclusions and has an option for another disease indication. In October 2018, the Company exercised its remaining option with REGENX for the additional disease indication and paid a $1.0 million fee for the exercise of the option. Each exercised option carries an annual maintenance fee of $0.1 million. In addition, for each option exercised, the Company is obligated to pay up to $9.0 million upon achievement of various milestones, as well as mid to high single-digit royalties on net sales of licensed products and mid single-digit to low double-digit percentage sublicenses fees, if any.

Bayer HealthCare LLC

The Company has an agreement with Bayer Healthcare LLC (Bayer) to research, develop and commercialize AAV gene therapy products for treatment of hemophilia A (DTX 201). Under this agreement, Bayer has been granted an exclusive license to develop and commercialize one or more novel gene therapies for hemophilia A. The agreement requires that Bayer use commercially reasonable efforts to conduct and fund a proof-of-concept (POC) clinical trial and any subsequent clinical trials and commercialization of gene therapy products for treatment of hemophilia A. Bayer will have worldwide rights to commercialize the potential future product.

Bayer is responsible to fund certain research and development services performed by the Company in the performance of its obligations under the annual research plan and budget. Under the terms of the agreement with Bayer, the Company is eligible to receive development and commercialization milestone payments of up to $232.0 million, as well as, royalty payments ranging in the high single-digit to low double-digit percentages, not exceeding the mid-teens, of net sales of licensed products. The Company achieved the first milestone in December 2017, the second milestone in April 2018, and has received $15.0 million for such milestones to date.

As of the acquisition date of Dimension on November 7, 2017, the Company valued the contract under ASC 805 and recorded an intangible asset of $13.5 million. The intangible asset was amortized to research and development expense over the research term and was completed in 2019. The Company recorded research and development expense of $0.2 million, $12.3 million, and $1.0 million for the years ended December 31, 2019, 2018, and 2017, respectively, for the amortization of the intangible asset.

The Company evaluated the agreement under ASC 606 and recorded a contract liability as of November 7, 2017 of $2.5 million. It was determined that the performance obligations under the agreement include (i) research and development services to be provided over the research term, (ii) a development and commercialization license, and (iii) the Company's participation in certain committees. It was determined that these performance obligations are not distinct in the context of the contract and therefore are a single performance obligation. The Company calculated the transaction price by including the unconstrained milestones along with the estimated payments for research and development services and recorded $0.5 million and $23.5 million, and $2.1 million as collaboration and license revenue for the years ended December 31, 2019, 2018, and 2017, respectively, by measuring the progress toward complete satisfaction of the performance obligation using an input measure. The performance obligation under the contract was substantially completed by end of 2019. As of December 31, 2019 and 2018, the Company had none and a $3.0 million contract asset associated with the performance obligation, respectively.

University of Pennsylvania

The Company has an agreement with University of Pennsylvania School of Medicine (Penn) to sponsor certain research related to liver and hemophilia gene therapy. In consideration for funding such research, Penn granted the Company an option to obtain a worldwide, non-exclusive or exclusive, royalty-bearing license, with the right to sublicense, under certain patent rights conceived, created or reduced to practice in the conduct of the research. The Company is required to reimburse Penn for filing, prosecuting and maintaining such patent rights unless and until the Company declines to exercise its option. Penn provides the Company with task-based, scientific reports of progress and results of the research, and granted the Company a royalty-free, nontransferable, non-exclusive right to copy and distribute any research reports furnished to the Company for any reasonable purpose, provided the results are not made publicly available until certain conditions are met, and the right to use, disclose and otherwise exploit the research results for any reasonable purpose, subject to similar restrictions on our public disclosure of the research results. Otherwise, the sponsored research agreement contains customary confidentiality provisions.

The Company also has a research, collaboration, and license agreement with Penn, which provides the terms for the Company and Penn to collaborate with respect to the pre-clinical development of gene therapy products for the treatment of certain indications. Under the agreement, Penn granted the Company an exclusive, worldwide license to certain patent rights arising out of the research program, subject to certain retained rights, and a non-exclusive, worldwide license to certain Penn intellectual property, in each case to research, develop, make, have made, use, sell, offer for sale, commercialize and import licensed products in each indication for the term of the agreement. The Company will fund the cost of the research program in accordance with a mutually agreed-upon research budget and will be responsible for clinical development, manufacturing and commercialization of each indication. The Company may be obligated to make milestone payments of up to $5.0 million for each indication, if certain development milestones are achieved over time, as well as low to mid-single digit royalties on net sales of each licensed product. The Company may also be obligated to make milestone payments of up to $25.0 million per approved product if certain commercial milestones are achieved.

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 are collaborating 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 has the primary responsibility for conducting certain research services, funded by the Company, and the Company will be responsible for development and commercialization costs. Pursuant to the agreement, the Company incurred $0.8 million, $1.9 million, and $4.3 million for the years ended December 31, 2019, 2018, and 2017, respectively, in research and development expense for the funding of certain research services received from Arcturus. As of December 31, 2019 and 2018, the Company has a balance of none and $0.5 million, respectively, in prepaid expenses and other current assets, and a balance of none and $0.4 million, respectively, in accrued liabilities related to Arcturus.

In June 2019, the Company entered into an Equity Purchase Agreement and an amendment to the Research Collaboration and License Agreement to expand the field of use and increase the number of disease targets to include mRNA, DNA and siRNA

therapeutics for up to 12 rare diseases. Pursuant to the agreements, the Company paid $6.0 million in cash upfront to Arcturus and purchased 2,400,000 shares of Arcturus' common stock at a stated value of $10.00 per share, resulting in a total of $30.0 million of consideration paid at the close of the transaction. As a result, the Company received expanded license rights; the Arcturus common stock; an option to purchase an additional 600,000 shares of Arcturus' common stock at $16.00 per share, which may be exercised up to two years after the agreement effective date, with certain restrictions; in addition to other changes as noted in the agreement. The period for the Company to exercise its option to purchase the additional stock may also be extended under certain circumstances as specified in the Equity Purchase Agreement. The Company is restricted from selling the 2,400,000 shares of common stock for a period of two years from the purchase date. The additional stock, if purchased, are also restricted from sale for a period of time as specified in the agreement. The Company also received the right to nominate one member to the Arcturus Board of Directors as well as one Board observer. Under the amended license agreement, certain early-stage milestone payments are reduced and the total potential milestone payments are increased due to the expanded number of targets. Arcturus is also entitled to reimbursement of related research expenses and royalties on commercial sales.

Immediately after the purchase, the Company held 18.2% of Arcturus' outstanding common stock, based on Arcturus' outstanding common stock balance as of the transaction date. The Company recorded the common stock investment at $13.9 million on the transaction date, which was based on the quoted market price on the closing date. As a result of the equity ownership and the right to nominate a board member, it was determined that the Company has significant influence over Arcturus. The Company elected to apply the fair value option to account for the equity investment in Arcturus. The Company also accounts for the option to purchase additional shares of Arcturus common stock at fair value, which was recorded at $0.5 million on the transaction date based on the Black-Scholes option pricing method. The remaining $15.6 million of the total $30.0 million paid as consideration was attributed to the additional license rights obtained and was recorded as in-process research and development expense.

The changes in the fair value of the Company's investment in Arcturus securities were as follows (in thousands):

	Arcturus common stock	Fair value of option to purchase additional shares of Arcturus common stock
December 31, 2018	$ —	$ —
Acquisition of investment in Arcturus securities	13,872	467
Change in fair value	12,216	1,197
December 31, 2019	$ 26,088	$ 1,664

GeneTx

In August 2019, the Company entered into a Program Agreement and a Unitholder Option Agreement with GeneTx Biotherapeutics, LLC (GeneTx) to collaborate on the development of GeneTx's GTX-102, an antisense oligonucleotide (ASO) for the treatment of Angelman syndrome.

Pursuant to the terms of the Unitholder Option Agreement, the Company made an upfront payment of $20.0 million for an exclusive option to acquire GeneTx. This option may be exercised any time prior to 30 days following notice of FDA acceptance of the IND for GTX-102 for an additional $50.0 million in payments. Alternatively, the Company may extend the option period by paying an option extension payment of $25.0 million. In the event the Company exercises the option extension, the Company has a right to acquire GeneTx for a payment of $125.0 million, at any time, until the earlier of 30 months from the first dosing of a patient in a planned Phase 1/2 study (subject to extensions) or 90 days after results are available from that study. This exclusive option to acquire GeneTx can be extended under certain circumstances, by up to four additional three-month periods, by paying an additional extension fee for each three-month period.

During the exclusive option period, GeneTx is responsible for conducting the program based on the development plan agreed between the parties and, subject to the terms in the Program Agreement, has the decision-making authority on all matters in connection with the research, development, manufacturing and regulatory activities with respect to the Program. The Company will provide support, at its discretion, including strategic guidance and clinical expertise. The Company and GeneTx will collaborate on the submission of the IND and management of the Phase 1/2 study in patients with Angelman syndrome. If the Company acquires GeneTx, the Company will then be responsible for all development and commercialization activities from the date of acquisition. The Company would also be required to make payments upon achievement of certain development and commercial milestones, as well as royalties, depending upon the success of the program.

Although GeneTx is a variable interest entity, the Company is not the primary beneficiary as it currently does not have the power to direct the activities that would most significantly impact the economic performance of GeneTx. Prior to product regulatory approval, all consideration paid to GeneTx represents rights to potential future benefits associated with GeneTx's in-process research and development activities, which have not reached technological feasibility and have no alternative future use. Accordingly, for the year ended December 31, 2019, the Company recorded the $20.0 million payment as an in-process research and development expense.

In February 2020, the Company paid $25.0 million upon acceptance of the IND to maintain its option to acquire GeneTx until the earlier of 30 months from the first dosing of a patient in the Phase 1/2 study (subject to extensions) or 90 days after results are available from that study.

9. Leases

As described in "Note 2. Summary of Significant Accounting Policies", the Company adopted *Topic 842* as of January 1, 2019. Prior period amounts have not been adjusted and continue to be reported in accordance with historic accounting under *Topic 840*.

The Company leases office space and research, testing and manufacturing laboratory space in various facilities in Novato and Brisbane, California, in Cambridge and Woburn, Massachusetts, and in certain foreign countries, under operating agreements expiring at various dates through 2028. Certain lease agreements include options for the Company to extend the lease for multiple renewal periods and also provide for annual minimum increases in rent, usually based on a consumer price index or annual minimum increases. None of these optional periods have been considered in the determination of the right-of-use lease asset or the lease liability for the leases as the Company did not consider it reasonably certain that it would exercise any such options. The Company recognizes lease expense on a straight-line basis over the non-cancelable term of its operating leases. The variable lease expense primarily consists of common area maintenance and other operating costs.

The Company recognizes rent expense on a straight-line basis over the noncancelable term of its operating leases. Prior to adoption of *Topic 842*, under *Topic 840*, rent expense was $6.4 million and $4.5 million during the years ended December 31, 2018 and 2017, respectively.

The components of lease expense were as follows (in thousands):

	Year Ended December 31, 2019
Operating lease expense	$ 9,163
Variable lease expense	2,779
Total	$ 11,942

Cash paid for amounts included in the measurement of lease liabilities for the year ended December 31, 2019 was $9.0 million and was included in net cash provided by operating activities in the Consolidated Statements of Cash Flows.

Future minimum lease payments under non-cancellable leases as of December 31, 2019 were as follows (in thousands):

Year Ending December 31,	Leases
2020	$ 9,786
2021	7,667
2022	7,521
2023	7,541
2024	5,571
Thereafter	7,582
Total future lease payments	45,668
Less: Amount representing interest	(8,676)
Present value of future lease payments	36,992
Less: Short-term lease liabilities	(7,235)
Long-term lease liabilities	$ 29,757

Lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. As of December 31, 2019, the weighted-average remaining lease term was 5.64 years and the weighted-average discount rate used to determine the lease liability was 7.5%.

10. Gain from Sale of Priority Review Vouchers

In January 2018, the Company completed the sale of a Rare Pediatric Disease Priority Review Voucher (PRV) it received in connection with the approval of Mepsevii for $130.0 million. In June 2018, the Company also completed the sale of the PRV it received in connection with the approval of Crysvita for $80.6 million, net, which was shared equally with KKC. As the PRVs did not have a carrying value, the gain recognized was equal to the net proceeds received. The Company recorded $170.3 million for its portion of the net proceeds for the year ended December 31, 2018 as a gain from the sale of the priority review vouchers.

11. Liability Related to the Sale of Future Royalties

In December 2019, the Company entered into a Royalty Purchase Agreement with RPI Finance Trust (RPI), an affiliate of Royalty Pharma. Pursuant to the agreement, RPI paid $320.0 million to the Company in consideration for the right to receive royalty payments effective January 1, 2020, arising from the net sales of Crysvita in the European Union, the United Kingdom, and Switzerland under the terms of the Company's Collaboration and License Agreement with KKC dated August 29, 2013, as amended. The agreement with RPI will automatically terminate, and the payment of royalties to RPI will cease, in the event aggregate royalty payments received by RPI are equal to or greater than $608.0 million prior to December 31, 2030, or in the event aggregate royalty payments received by RPI are less than $608.0 million prior to December 31, 2030, when aggregate royalty payments received by RPI are equal to $800.0 million.

As RPI's rate of return is explicitly limited due to the cap on royalties they may receive, proceeds from the transaction was recorded as a liability (liability related to sale of future royalties on the Consolidated Balance Sheets). The Company will amortize $320.0 million, net of transaction cost of $5.8 million using the effective interest method over the estimated life of the arrangement. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future royalty payments to be received by the Company and paid to RPI, subject to the capped amount, over the life of the arrangement. The aggregate future estimated royalty payments (subject to the capped amount), less the $314.2 million of net proceeds, will be recorded as non-cash interest expense over the life of the arrangement. Consequently, the Company estimates an imputed interest on the unamortized portion of the liability and records interest expense relating to the transaction. The Company will continue to record the royalty revenue rising from the net sales of Crysvita in the applicable European territories as non-cash royalty revenue in the Consolidated Statements of Operations over the term of the arrangement.

The Company periodically assesses the expected royalty payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than the Company's initial estimates or the timing of such payments is materially different than its original estimates, the Company will prospectively adjust the amortization of the liability and the effective interest rate. Through December 31, 2019, the Company's effective annual interest rate was approximately 10.1%.

There are a number of factors that could materially affect the amount and timing of royalty payments from KKC in the applicable European territories, most of which are not within the Company's control. Such factors include, but are not limited to, the success of KKC's sales and promotion of Crysvita, changing standards of care, the introduction of competing products, approval of label expansion for adults, pricing for reimbursement in various European territories, manufacturing or other delays, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of Crysvita, significant changes in foreign exchange rates as the royalty payments are made in U.S. dollars (USD) while significant portions of the underlying European sales of Crysvita are made in currencies other than USD, and other events or circumstances that could result in reduced royalty payments from European sales of Crysvita, all of which would result in a reduction of non-cash royalty revenue and the non-cash interest expense over the life of the arrangement. Conversely, if sales of Crysvita in Europe are more than expected, the non-cash royalty revenue and the non-cash interest expense recorded by the Company would be greater over the term of the arrangement.

The Company will record non-cash royalty revenues and non-cash interest expense within its Consolidated Statements of Operations over the term of the arrangement. The following table shows the activity within the liability account during the year ended December 31, 2019 (in thousands):

	December 31, 2019
Liability related to the sale of future royalties — beginning balance	$ —
Proceeds from sale of future royalties	314,234
Non-cash interest expense	1,135
Liability related to the sale of future royalties at end of year	$ 315,369

12. Equity

At-the-Market Offerings

In July 2016, the Company entered into an At-The-Market (ATM) sales agreement with Cowen and Company, LLC (Cowen), whereby the Company sold $150.0 million in aggregate proceeds of common stock, through Cowen as our sales agent. During the year ended December 31, 2017, the Company sold 912,351 shares of common stock, resulting in net proceeds of approximately $67.6 million, after commissions and other offering costs.

In July 2017, the Company entered into an additional ATM sales agreement with Cowen whereby the Company may sell up to $150.0 million in aggregate proceeds of common stock from time to time, through Cowen as its sales agent. During the years ended December 31, 2019, 2018, and 2017, the Company sold 468,685, 640,257, and 1,338,866 shares of common stock, respectively, resulting in net proceeds of approximately $24.8 million, $38.1 million, and $64.3 million, respectively, after commissions and other offering costs.

Underwritten Public Offering

In January 2018, the Company completed an underwritten public offering in which 5,043,860 shares of common stock were sold, which includes 657,895 shares purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of $57.00 per share. The total proceeds that the Company received from the offering were approximately $271.0 million, net of underwriting discounts and commissions.

In February 2019, the Company completed an underwritten public offering in which 5,833,333 shares of common stock were sold, which included 760,869 shares purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of $60.00 per share. The total proceeds that the Company received from the offering were approximately $330.4 million, net of underwriting discounts and commissions.

Common Stock Warrants

As of December 31, 2019 and 2018, there was an aggregate of 149,700 of common stock warrants outstanding with exercise price of $3.01 and expiration dates in 2020 and 2021.

13. Stock-Based Awards

Equity Plan Awards

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. In 2014, the Company adopted the 2014 Incentive Plan (the 2014 Plan). 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. No further grants subsequent to the IPO were made under the 2011 Plan. The 2014 Plan provides for automatic annual increases in shares available for grant, beginning on January 1, 2015 through January 1, 2024. Under the terms of the 2014 Plan, awards 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 awards must be at least 110% of fair market of the common stock on the grant date, as determined by the board of directors. The term of an award granted under the 2014 Plan may not exceed ten years. Typically, the vesting schedule for option grants to the employees provides that 1/4 of the grant vests upon the first anniversary of the date of grant, with the remainder of the shares vesting monthly thereafter at a rate of 1/48 of the total shares subject to the option. The vesting schedule for RSU grants provides that 1/4 of the grant vests upon the annual anniversary of the date of grant over the period of four years.

As part of the acquisition of Dimension (discussed in “Note 3. Dimension Acquisition”), the Company assumed an equivalent 639,897 options to purchase shares of common stock of the Company from the equity plans of Dimension. No further grants subsequent to the acquisition are available under these equity plans.

As of December 31, 2019, an aggregate of 10,521,371 shares of common stock have been authorized for issuance under the 2011 Plan, the 2014 Plan, and the assumed equity awards from the Dimension plans.

Stock Option Activity

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

	Options Outstanding			
	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding — December 31, 2016	4,429,472	$ 61.85	8.22	$ 79,135
Options granted	1,328,860	71.99		
Options assumed	639,897	27.97		
Options exercised	(478,470)	16.25		
Options cancelled	(520,349)	78.70		
Outstanding — December 31, 2017	5,399,410	$ 62.75	7.40	$ 37,687
Options granted	1,479,451	55.54		
Options exercised	(713,263)	36.21		
Options cancelled	(812,474)	74.80		
Outstanding — December 31, 2018	5,353,124	$ 62.46	7.22	$ 23,243
Options granted	1,762,075	63.03		
Options exercised	(235,678)	32.87		
Options cancelled	(766,457)	72.48		
Outstanding — December 31, 2019	6,113,064	$ 62.51	7.00	$ 18,989
Vested and exercisable — December 31, 2019	3,429,579	$ 63.14	5.83	$ 18,514
Vested and expected to vest — December 31, 2019	5,847,778	$ 62.58	6.92	$ 18,945

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. The total intrinsic value of options exercised during the years ended December 31, 2019, 2018, and 2017 was $6.5 million, $22.9 million and $20.4 million, respectively. Cash received from the exercise of options was $7.7 million, $25.8 million, and $7.8 million as of December 31, 2019, 2018, and 2017, respectively.

The weighted-average estimated fair value of stock options granted was $37.15, $33.32 and $44.20 per share of the Company's common stock during the years ended December 31, 2019, 2018, and 2017, respectively. The total estimated grant date fair value of options vested during the years ended December 31, 2019, 2018, and 2017 was $45.3 million, $51.7 million, and $49.1 million, respectively.

Restricted Stock Units

The following table summarizes activity under the Company's Restricted Stock Units (RSUs) from the 2014 Plan and related information:

	RSUs Outstanding	
	Number of Shares	Weighted- Average Grant Date Fair Value
Unvested — December 31, 2016	573,744	$ 71.45
RSUs granted	516,161	71.58
RSUs vested	(156,021)	71.93
RSUs cancelled	(112,324)	76.78
Unvested — December 31, 2017	821,560	$ 70.71
RSUs granted	555,905	56.01
RSUs vested	(235,913)	71.01
RSUs cancelled	(187,475)	65.37
Unvested — December 31, 2018	954,077	$ 63.12
RSUs granted	863,065	62.78
RSUs vested	(313,682)	66.25
RSUs cancelled	(205,310)	64.28
Unvested — December 31, 2019	1,298,150	$ 61.96

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 one to four years. The total grant date fair value of the 313,682 shares vested during 2019 was approximately $20.8 million with an aggregate intrinsic value of the shares of $18.4 million.

Performance Stock Units

In December 2017, the Company began granting performance stock units (PSUs) to certain employees. The following table summarizes activity under the Company's PSUs from the 2014 Plan and related information:

	PSUs Outstanding	
	Number of Shares	Weighted- Average Grant Date Fair Value
Unvested — December 31, 2016	—	$ —
PSUs granted	508,850	48.03
Unvested — December 31, 2017	508,850	$ 48.03
PSUs granted	71,725	59.67
PSUs cancelled	(97,375)	48.58
Unvested — December 31, 2018	483,200	$ 49.65
PSUs granted	61,500	67.31
PSUs vested	(65,643)	48.03
PSUs cancelled	(79,517)	50.01
Unvested — December 31, 2019	399,540	$ 52.56

The fair value of the PSUs is determined on the grant date based on the fair value of the Company's common stock. PSUs are subject to vest only if certain specified criteria are achieved and the employees' continued service with the Company after achievement of the specified criteria. For certain PSUs, the number of PSUs that may vest are also subject to the achievement of certain specified criteria. As of December 31, 2019, the specified criteria were deemed probable of achievement or already achieved. Stock-based compensation for these PSUs is recognized over the service period beginning in the period the Company determines it is probable that the performance criteria will be achieved. The total grant date fair value of the 65,643 shares vested during 2019 was approximately $3.2 million with an aggregate intrinsic value of the shares of $4.2 million.

Employee Stock Purchase Plan

In January 2014, the Company adopted the 2014 Employee Stock Purchase Plan (ESPP) and reserved a total of 600,000 shares of common stock for issuance under the ESPP. The ESPP provides for automatic annual increases in shares available for grant, beginning on January 1, 2015 through January 1, 2024. Eligible employees may purchase common stock at 85% of the lesser of the fair market value of common stock on the offering date or the purchase date with a six-month look-back feature. ESPP purchases are settled with common stock from the ESPP's previously authorized and available pool of shares. During the year ended December 31, 2019, the Company issued 85,845 shares of common stock under the ESPP. As of December 31, 2019, an aggregate of 2,933,325 shares of common stock have been authorized for future issuance on the ESPP.

Stock-Based Compensation Expense

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

	Year Ended December 31,		
	2019	2018	2017
Cost of sales	$ 1,084	$ 146	$ —
Research and development	44,205	45,572	38,212
Selling, general and administrative	36,706	34,389	29,802
Total stock-based compensation expense	$ 81,995	$ 80,107	$ 68,014

Stock-based compensation of $1.4 million and $1.1 million was capitalized into inventory for the years ended December 31, 2019 and 2018, respectively. There was no stock-based compensation capitalized for the year ended December 31, 2017. Capitalized stock-based compensation is recognized as cost of sales when the related product is sold. As of December 31, 2019, the total unrecognized compensation expense related to unvested equity awards, net of estimated forfeitures, was $133.0 million, which the Company expects to recognize over an estimated weighted-average period of 2.40 years. In determining the estimated fair value of the stock options and ESPP, 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—The Company's expected volatility is based on historical volatility over the look-back period corresponding to the expected term.

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.

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

	Year Ended December 31,		
	2019	2018	2017
Expected term (years)	6.22	6.23	6.23
Expected volatility	61%	62%	65%
Risk-free interest rate	2.4%	2.7%	2.1%
Expected dividend rate	0.0%	0.0%	0.0%

14. Defined Contribution Plan

The Company sponsors a retirement plan in which substantially all of its full-time employees in the United States and certain other foreign countries are eligible to participate. Eligible participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. The Company recorded $3.6 million, $2.9 million, and $2.1 million as contribution expenses for the years ended December 31, 2019, 2018, and 2017, respectively.

15. Income Taxes

The components of the Company's loss before income taxes were as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Domestic	$ 399,709	$ 205,440	$ 250,917
Foreign	(265)	(8,343)	67,421
Total loss before income taxes	$ 399,444	$ 197,097	$ 318,338

The components of the Company's income tax provision were as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Current provision for income taxes:			
Federal	$ —	$ —	$ —
State	51	14	5
International	1,092	500	42
Total current tax provision	1,143	514	47
Deferred tax provision (benefit):			
Federal	—	—	(16,243)
State	2,140	—	(3)
International	—	—	—
Total deferred tax provision (benefit)	2,140	—	(16,246)
Total provision for (benefit from) income taxes	$ 3,283	$ 514	$ (16,199)

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:

	Year Ended December 31,		
	2019	2018	2017
Federal statutory income tax rate	21.0 %	21.0 %	34.0 %
State income taxes, net of federal benefit	(0.5)	—	—
Federal tax credits	5.2	9.5	9.0
Other	(0.2)	(0.2)	(0.9)
Nondeductible permanent items	(0.4)	(0.8)	—
Stock-based compensation	(1.0)	(0.8)	(0.6)
Uncertain tax positions	(1.0)	(1.9)	(1.8)
Change in valuation allowance	(23.6)	(26.8)	(32.5)
Foreign rate differential	(0.3)	(0.3)	(7.2)
Change in federal tax rate	—	—	5.1
Provision for income taxes	(0.8) %	(0.3) %	5.1 %

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

	Year Ended December 31,	
	2019	2018
Deferred tax assets:		
Loss carryforwards	$ 185,892	$ 183,331
Tax credits	158,791	137,019
Stock options	40,676	29,925
Accruals and reserves	19,622	7,418
Fixed assets and intangibles	3,870	2,820
Liability related to sale of future royalties	81,424	—
Other	4,183	1,189
Gross deferred tax assets	494,458	361,702
Valuation allowance	(486,796)	(361,702)
Total deferred tax assets	7,662	—
Deferred tax liabilities:		
In-process research and development	(33,306)	(31,166)
Right-of-use lease assets	(7,662)	—
Gross deferred tax liabilities	(40,968)	(31,166)
Net deferred tax asset (liabilities)	$ (33,306)	$ (31,166)

As of December 31, 2019 and 2018, the Company had $549.9 million and $558.3 million of federal net operating loss carryforwards available to reduce future taxable income that will begin to expire in 2032. As of December 31, 2019 and 2018, the Company had $520.2 million and $476.8 million of state net operating loss carryforwards available to reduce future taxable income that will begin to expire in 2031.

As of December 31, 2019 and 2018, the Company had federal research tax credit carryforwards of $11.7 million and $7.5 million available to reduce future tax liabilities that will begin to expire in 2030. As of December 31, 2018 and 2017, the Company had state research credit carryforwards of $25.5 million and $17.3 million available to reduce future tax liabilities that will be carried forward indefinitely.

As of December 31, 2019 and 2018, the Company had federal Orphan Drug Credits of $160.0 million and $143.5 million available to reduce future tax liabilities that will begin to expire in 2031.

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, $3.6 million of federal net operating loss carryforwards, $3.6 million of state net operating loss carryforwards, and $0.2 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.

On November 7, 2017, the Company acquired Dimension (see “Note 3. Dimension Acquisition”). The Company recorded a net $47.4 million deferred tax liability relating to the tax impact of future GAAP amortization or potential impairments associated with the identified intangible assets acquired, which are indefinitely lived assets and are not currently deductible for tax purposes. Due to the reduction of the US corporate tax rate to 21% in the period subsequent to the acquisition, the Company recorded a net decrease to the deferred tax liability of $16.2 million with a corresponding benefit from income taxes of $16.2 million for the year ended December 31, 2017. Due to a change in the state tax rates, the Company recorded a net increase to the deferred tax liability of $2.1 million with a corresponding deferred income tax expense of $2.1 million for the year ended December 31, 2019.

The valuation allowance increased by $125.1 million and $57.5 million during the year ended December 31, 2019 and 2018, respectively.

The Company recorded unrecognized tax benefits for uncertainties in income taxes. A reconciliation of the Company's unrecognized tax benefits follows (in thousands):

	December 31,		
	2019	2018	2017
Balance at beginning of year	$ 33,727	$ 28,377	$ 13,505
Additions based on tax positions related to current year	5,575	4,750	9,338
Additions for tax positions of prior years	652	600	5,534
Reductions for tax positions of prior years	—	—	—
Balance at end of year	$ 39,954	$ 33,727	$ 28,377

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, 2019 and 2018, 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 year.

It is our intention to reinvest the earnings of our non-U.S. subsidiaries in their operations. As of December 31, 2019, the Company had not made a provision for any incremental foreign withholding taxes on approximately $2.1 million of the excess of the amount of net income for financial reporting over the tax basis of investments in foreign subsidiaries that are essentially permanent in duration. If these earnings were repatriated to the U.S., the deferred tax liability associated with these temporary differences would result in a nominal amount of withholding taxes.

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, 2019 remain subject to examination.

16. Commitments and Contingencies

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, 2019, the aggregate payments under contractually binding manufacturing and service agreements are as follows (in thousands):

Year Ending December 31,	Manufacturing and Services
2020	7,854
2021	461
Thereafter	—
	$ 8,315

See "Note 9. Leases" for lease commitments.

Contingencies

While there are no material 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.

17. Net Loss per Share

The following table sets forth the computation of the basic and diluted net loss per share during the years ended December 31, 2019, 2018, and 2017 (in thousands, except share and per share data):

	Year Ended December 31,		
	2019	2018	2017
Numerator:			
Net loss	$ (402,727)	$ (197,611)	$ (302,139)
Denominator:			
Weighted-average shares used to compute net loss per share, basic and diluted	56,576,885	49,775,223	42,453,135
Net loss per share, basic and diluted	$ (7.12)	$ (3.97)	$ (7.12)

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

	Year Ended December 31,		
	2019	2018	2017
Options to purchase common stock, RSUs, and PSUs	7,978,666	7,301,431	5,862,784
Employee stock purchase plan	3,953	3,345	2,728
Common stock warrants	149,700	149,700	149,700
	8,132,319	7,454,476	6,015,212

18. Accumulated Other Comprehensive Loss

Total accumulated other comprehensive loss consisted of the following (in thousands):

	Year Ended December 31,	
	2019	2018
Cumulative foreign currency translation adjustment	$ (306)	$ (329)
Unrealized gain (loss) on securities available-for-sale	159	(304)
Total accumulated other comprehensive loss	$ (147)	$ (633)

19. 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 per share data):

	2019			
	March 31,	June 30,	September 30,	December 31,
Revenue	$ 18,172	$ 24,149	$ 25,800	$ 35,593
Operating expenses	$ 117,386	$ 136,623	$ 143,833	$ 130,045
Net loss	$ (96,756)	$ (99,172)	$ (112,994)	$ (93,805)
Net loss per share, basic and diluted	$ (1.82)	$ (1.72)	$ (1.96)	$ (1.62)

	2018			
	March 31,	June 30,	September 30,	December 31,
Revenue	$ 10,677	$ 12,794	$ 11,763	$ 16,261
Operating expenses	$ 107,164	$ 107,694	$ 101,409	$ 106,601
Net income (loss)	$ 30,253	$ (52,728)	$ (87,310)	$ (87,826)
Net income (loss) per share, basic	$ 0.63	$ (1.06)	$ (1.74)	$ (1.73)
Net income (loss) per share, diluted	$ 0.62	$ (1.06)	$ (1.74)	$ (1.73)

Exhibit 4.3

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following description of the capital stock of Ultragenyx Pharmaceutical Inc. ("Ultragenyx") does not purport to be complete and is subject to, and qualified in its entirety by, our amended and restated certificate of incorporation ("certificate") and our amended and restated bylaws ("bylaws"), each of which is incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this exhibit is a part.

General

Our authorized capital stock consists of 250,000,000 shares of common stock, $0.001 par value, and 25,000,000 shares of preferred stock, $0.001 par value per share. We have one class of securities registered under Section 12 of the Securities Exchange Act of 1934, our common stock, which is listed on the Nasdaq Global Select Market under the symbol "RARE."

Common Stock

Voting rights. The holders of our common stock are entitled to one vote per share on all matters submitted to a vote of stockholders. A plurality of the votes cast is required for stockholders to elect directors. All other matters put to a stockholder vote generally require the approval of a majority of the votes cast, except as otherwise provided by our certificate or bylaws or required by law. Stockholders do not have cumulative voting rights.

Dividends. The holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding.

Liquidation. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding.

Preemptive, subscription and conversion rights. Our common stock is not redeemable and has no preemptive, subscription or conversion rights.

Transfer agent. The transfer agent and registrar for our common stock is the American Stock Transfer & Trust Company

The rights, preferences and privileges of holders of our common stock are subject to the rights of the holders of shares of any series of preferred stock which we may issue.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 25,000,000 shares of preferred stock, none of which are outstanding. Our board of directors may issue preferred stock in one or more series and fix the rights, preferences, privileges and restrictions of such preferred stock, including:

- dividend rights;
- dividend rate;
- conversion rights;
- voting rights;
- rights and terms of redemption;
- redemption price or prices;

- the liquidation preferences of any wholly unissued series of preferred stock; and
- the number of shares constituting any series or the designation of such series.

The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to the holders of our common stock or adversely affect the rights and powers, including voting rights, of the holders of our common stock.

Anti-Takeover Provisions

Some provisions of our certificate, bylaws and Delaware law may have the effect of delaying, discouraging or preventing a change in control of us or changes in our management. Pursuant to our certificate and bylaws:

- the board of directors is authorized to issue “blank check” preferred stock without stockholder approval;
- the board of directors is classified, with members serving staggered three-year terms;
- vacancies on the board of directors may be filled only by the board of directors;
- stockholders may remove directors only for cause;
- the board of directors is expressly authorized to make, alter or repeal any provision of our bylaws;
- stockholders may amend our bylaws and specified provisions of our certificate only with the affirmative vote of the holders of 75% of the voting power of the common stock outstanding and entitled to vote on the matter;
- stockholders may not cumulate votes in the election of directors;
- stockholders may take action only at a duly called meeting of the stockholders, and stockholders are not permitted to act by written consent;
- special meetings of the stockholders may be called only by the board of directors or the chairman of the board;
- stockholders must satisfy advance notice procedures to submit proposals or nominate directors for consideration at a stockholders meeting; and
- we will indemnify officers and directors against losses that they may incur as a result of investigations and legal proceedings resulting from their services to us, which may include services in connection with takeover defense measures.

In addition, we are subject to the provisions of Section 203 of the Delaware General Corporation Law (“DGCL”). In general, the statute prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years after the date that the person became an interested stockholder unless, with some exceptions, the business combination or the transaction in which the person became an interested stockholder is approved in a prescribed manner. Generally, a “business combination” includes a merger, asset or stock sale or other transaction resulting in a financial benefit to the stockholder, and an “interested stockholder” is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of the corporation’s outstanding voting stock. This provision may have the effect of delaying, deferring or preventing a change in control without further action by the stockholders.

Exclusive Forum

Our certificate provides that unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer, employee or agent of Ultragenyx or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the DGCL, or our restated certificate of incorporation or our amended and restated bylaws; or (iv) any action asserting a claim against us or any of our directors, officers, employees or agents governed by the internal affairs doctrine. Our certificate also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Exhibit 10.10

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED

AMENDMENT NO. 9 TO COLLABORATION AND LICENSE AGREEMENT

This Amendment No. 9 to the Collaboration and License Agreement ("***Amendment***") is made and entered into by and between Kyowa Kirin Co., Ltd. (formerly, Kyowa Hakko Kirin Co., Ltd.), a company organized and existing under the laws of Japan, with an address at 1-9-2 Otemachi, Chiyoda-ku, Tokyo, 100-0004, Japan ("***KKC***") and Ultragenyx Pharmaceutical Inc., a company organized and existing under the laws of the State of Delaware, with an address at 60 Leveroni Court, Novato, California 94949, USA ("***UGNX***").

RECITALS

A. WHEREAS, KKC and UGNX entered into a Collaboration and License Agreement effective as of August 29, 2013, an Amendment No. 1 to Collaboration and License Agreement effective as of August 24, 2015, an Amendment No. 2 to Collaboration and License Agreement effective as of November 28, 2016, an Amendment No. 3 to Collaboration and License Agreement effective as of September 29, 2017, an Amendment No. 4 to Collaboration and License Agreement effective as of January 29, 2018, an Amendment No. 5 to Collaboration and License Agreement effective as of April 30, 2018, an Amendment No. 6 to Collaboration and License Agreement effective as of February 1, 2019, an Amendment No. 7 to Collaboration and License Agreement effective as of December 5, 2018, and an Amendment No. 8 to Collaboration and License Agreement effective as of July 4, 2019 (collectively, the "***Collaboration Agreement***").

B. WHEREAS, both Parties wish to further amend the Collaboration Agreement as set forth below.

C. NOW, THEREFORE, in consideration of the mutual covenants and premises herein contained, the Parties agree as follows:

1. This Amendment shall be effective as of December 23, 2019 (the "***Amendment Effective Date***").

2. Any capitalized terms that are not defined in this Amendment will have their respective meanings set forth in the Collaboration Agreement.

3. Section 7.6 of the Collaboration Agreement is hereby deleted in its entirety and replaced with the following:

*"**7.6*** ***Taxes.***

7.6.1 ***Tax Liabilities***. *Except as provided to the contrary in Section 7.6.3(e) or otherwise in this Agreement, each Party shall be solely responsible for any and all Taxes, including, but not limited to, direct Taxes, indirect Taxes, or Taxes withheld at the source, together with related interest and penalties, if any, imposed by any government tax authority based upon the facts, circumstances, and requirements of such Party in respect of amounts arising from this Agreement. In the event a Party receives a deficiency notice or similar correspondence from a government tax authority, the Party whose facts and circumstances, structure, or tax position (other than in its capacity as a Withholding Party) resulted in the imposition of the Tax giving rise to the deficiency notice (the "**Liable Party**") shall be responsible for payment of the deficiency regardless of whether it is the Party that receives the deficiency notice. Any Party that receives a deficiency notice, a notice of audit or investigation or any similar proceeding or notice (a "**Tax Notice**") shall use Commercially Reasonable Efforts to give notice to the Liable Party within ten (10) days of receiving such Tax Notice; provided, however, that failure to provide notice to the Liable Party shall not relieve the Liable Party of its obligations hereunder so long as the Liable Party is not materially prejudiced by the failure to provide such notice. If there is a refund of all or any portion of any Tax paid or otherwise economically borne by the Liable Party, such refund shall be paid to the Liable Party. Where a Party pays or otherwise economically bears a liability for which the other Party is responsible hereunder, the responsible Party shall indemnify such other Party with respect to such liability.*

7.6.2 ***Tax Payments, Taxes Withheld at the Source, and Deficiencies.*** *The Parties shall reasonably cooperate in completing and filing documents required under the provisions of any Applicable Laws in connection with the making of any required Tax payments or payments of Tax withheld at the source, or in connection with any claim to an exemption from, reduction of, or a refund or credit for any such payments to the extent available under Applicable Laws. If a Party or any of its Affiliates is required by Applicable Laws to deduct or withhold any Taxes as a result of this Agreement (the "**Withholding Party**"), then the Withholding Party shall make such deduction or withholding and pay the full amount deducted or withheld to the relevant government tax authority in accordance with Applicable Laws. In this event, the Withholding Party shall promptly furnish the Liable Party with reasonable evidence of such deduction or withholding and payment thereof to the relevant government tax authority in electronic or written form. If it is determined that a Withholding Party was required by Applicable Laws to deduct or withhold any such Taxes as a result of this Agreement but the Withholding Party did not deduct or withhold such Taxes, the Withholding Party shall have the right to make such deduction or withholding from any future payments made under this Agreement, pay the full amount deducted or withheld to the government tax authority in accordance with Applicable Laws, and to take any other actions required to comply with Applicable Laws. To the extent future payments under this Agreement are insufficient to satisfy payments of such Taxes within the time requirement of the government tax authority, then the Liable Party shall indemnify the Withholding Party in an amount required to fully satisfy such Tax payments, including any related penalty and interests, within the*

time requirement of the government tax authority. Deficiency interest and penalties, if any, with respect to Tax payments including Tax withholding payments shall be borne by the Liable Party.

7.6.3 ***Treatment of Royalties and Revenue Shares for Tax Purposes****.*

*(a) To the extent permitted by Applicable Laws, the Parties agree to treat for income Tax purposes the revenue shares payable pursuant to Section [***] and subsections [***], [***], [***], [***] and [***] of Section [***] as [***] within the meaning of Article 12 of the Income Tax Convention for the Avoidance of Double Taxation between [***] and [***] ("[***] **Treaty**") as consideration for the use of, or the right to use, a patent or patents, a secret process, or information concerning industrial, commercial or scientific experience within the meaning of [***] Treaty and any equivalent income tax treaties that may apply to such payments.*

(b) To the extent permitted by Applicable Laws, the Parties agree to treat for income Tax purposes the revenue shares payable pursuant to Section [***] as [***].

*(c) To the extent permitted by Applicable Laws, the Parties agree to treat for income Tax purposes the revenue shares payable pursuant to Section [***]and subsections [***], [***], [***] and [***] of Section [***] as [***] within the meaning of Article 12 of the Income Tax Convention for the Avoidance of Double Taxation between [***] and [***] ("[***] **Treaty**") as consideration for the use of, or the right to use, a patent or patents, a secret process, or information concerning industrial, commercial or scientific experience within the meaning of [***] Treaty and any equivalent income tax treaties that may apply to such payments.*

(d) For the avoidance of doubt, the Parties do not intend for this Agreement to [***] for U.S. income tax purposes between the Parties and/or their Affiliates in respect of the [***] in Section [***] and [***]. The Parties shall file all tax returns in a manner consistent with such tax treatment, except as may be required by Applicable Laws.

(e) If the Internal Revenue Service (or a U.S. state or local tax authority) asserts that [***](such [***], a "[***]"), or [***] at any time, in respect of this Agreement or [***] in Section [***], the following costs relating to such audit or other controversy shall be borne by [***] and/or its affiliates: (i) any Taxes (including any applicable interest, additions to Tax or penalties) imposed by the Internal Revenue Service (or a U.S. state or local tax authority) directly relating solely to its assertion that [***] and (ii) any professional fees relating to the [***] of this Agreement or such [***], including, but in no way limited to, professional fees relating to the [***] and filing of tax returns. Notwithstanding the foregoing, and for the avoidance of doubt, any Taxes that would have been imposed in the absence of any such [***] shall not be governed by this paragraph 7.6.3(e) but

shall be borne in accordance with Sections 7.6.1 and 7.6.2. If the Internal Revenue Service (or a U.S. state or local tax authority) asserts that [***], in respect of the [***] in Section [***], KKC and/or its affiliates shall have the sole authority to conduct, and undertake the defense of, such tax audit or other tax controversy, including the settlement and resolution of any such tax audit or other tax controversy (and KKC and/or its affiliates shall bear any and all expenses related thereto), except to the extent any tax audit or tax controversy could reasonably be expected to adversely impact the other Party, in which case both Parties shall have joint authority to conduct, and undertake the defense of, such tax audit or tax controversy and each Party shall bear its own respective costs associated with such tax audit or tax controversy.

(f) If the Internal Revenue Service were to assert that any arrangement pursuant to this Agreement were to [***], the parties agree that Kyowa Kirin, Inc. will be designated the "[***]" of such [***] within the meaning of Section [***] of the Internal Revenue Code of 1986, as amended (and [***] and provisions of state, local or non-U.S. law). If an audit relates to a year prior to 2018, KKC shall act as the "[***]" with respect to such tax matters.

7.6.4. ***Cooperation and Costs****. The Parties will coordinate and cooperate fully with each other in exchanging information and providing such assistance as the other Party may reasonably request in connection with any Tax Notice, filings, investigation, audits, examinations or other inquiries, appeals, or litigation by a taxing authority relating to this Agreement. Except as otherwise provided in Section 7.6.3(e), the Liable Party, if there is only one, shall have the sole authority to conduct, and undertake the defense of, any tax audits or other tax controversies, including the settlement and resolution of any tax audits or other tax controversies, except to the extent any tax audit or tax controversy adversely impacts the other Party or if both Parties are potentially Liable Parties, in which case both Parties shall have joint authority to conduct, and undertake the defense of, such tax audit or tax controversy and each Party shall bear its own respective costs associated with such tax audit or tax controversy. Any other costs associated with any filings, investigations, audits, examinations or other inquiries, appeals or litigation, other than the Tax liability and the costs discussed in the preceding sentence, shall be borne by the Liable Party, except as otherwise provided in Section 7.6.3(e)."*

4. Except as expressly provided in this Amendment, all other terms, conditions and provisions of the Collaboration Agreement shall continue in full force and effect as provided therein.

5. This Amendment may be executed in identical duplicate copies exchanged by facsimile or e-mail (PDF form) transmission. The Parties agree to execute two identical original copies of this Amendment after exchanging signed facsimile versions. Each identical counterpart will be deemed an original, but all of which together will constitute one and the same instrument.

[Signatures on Following Page]

IN WITNESS WHEREOF, the Parties have executed this Amendment No. 9 to Collaboration and License Agreement to be effective as of the Amendment Effective Date.

KYOWA KIRIN CO., LTD.	**ULTRAGENYX PHARMACEUTICAL INC.**
By: /s/ Yasuo Fujii	By: /s/ Thomas Kassberg
Name: Yasuo Fujii	Name: Thomas Kassberg
Title: Director, Business Development Dept.	Title: Chief Business Officer

Exhibit 10.25

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED

Royalty Purchase Agreement

By and Between

Ultragenyx Pharmaceutical Inc.

and

RPI Finance Trust

Dated as of December 17, 2019

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ROYALTY PURCHASE AGREEMENT

This ROYALTY PURCHASE AGREEMENT, dated as of December 17, 2019 (this "Agreement"), is made and entered into by and between Ultragenyx Pharmaceutical Inc., a Delaware corporation (the "Seller"), on the one hand, and RPI Finance Trust, a Delaware statutory trust (the "Buyer"), on the other hand.

W I T N E S S E T H:

WHEREAS, pursuant to the License Agreement, the Seller and Licensee granted to each other certain licenses and other rights and Licensee retained the exclusive right to (among other activities) sell the Licensed Product in the European Territory, and Licensee, in partial consideration thereof, agreed to pay the Royalty and other payments to the Seller; and

WHEREAS, the Buyer desires to purchase the Royalty from the Seller, and the Seller desires to sell the Royalty to the Buyer.

NOW THEREFORE, in consideration of the representations, warranties, covenants and agreements set forth herein and for good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, the Seller and the Buyer hereby agree as follows:

ARTICLE 1
DEFINED TERMS AND RULES OF CONSTRUCTION

Definitions

. As used in this Agreement, the following terms shall have the following meanings:

"Affiliate" shall have the meaning ascribed to the term Affiliate in Section 1.1.1 of the License Agreement.

"Agreement" is defined in the preamble.

"Amendment No. 3" means that certain Amendment No. 3 to the Collaboration and License Agreement by and between the Seller and Licensee, dated as of September 29, 2017.

"Applicable Patents" is defined in Section 6.12(c).

"Bankruptcy Laws" means, collectively, bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, fraudulent transfer or other similar laws affecting the enforcement of creditors' rights generally.

"Bill of Sale" is defined in Section 3.3.

"Business Day" means any day other than (i) a Saturday or Sunday or (ii) a day on which banking institutions located in New York are permitted or required by applicable law or regulation to remain closed.

"Buyer" is defined in the preamble.

"Buyer Closing Certificate" is defined in Section 3.2(b).

"Buyer Indemnified Parties" is defined in Section 8.1(a).

"Closing" is defined in Section 3.1.

"Closing Date" means the date on which the Closing occurs.

"Data Room" is defined in Section 3.9.

"Disclosure Schedule" means the Disclosure Schedule, dated as of the date hereof, delivered to the Buyer by the Seller concurrently with the execution of this Agreement.

"Distribution Agreement" means that certain License and Distribution Agreement by and between [***] and Seller, dated as of May 22, 2017.

"Drug Substance" shall have the meaning ascribed to the term Drug Substance in Section 1.1.15 of the License Agreement.

"European Territory" shall have the meaning ascribed to the term European Territory in Section 1.1.18 of the License Agreement and for purposes of this Agreement and the License Agreement shall: (i) include the United Kingdom and Switzerland and (ii) exclude the Republic of Turkey.

"Field" shall have the meaning ascribed to the term Field in Section 1.1.22 of the License Agreement.

"Governmental Entity" means any: (i) nation, principality, republic, state, commonwealth, province, territory, county, municipality, district or other jurisdiction of any nature; (ii) federal, state, local, municipal, foreign or other government; (iii) governmental or quasi-governmental authority of any nature (including any governmental division, subdivision, department, agency, bureau, branch, office, commission, council, board, instrumentality, officer, official, representative, organization, unit, body or other entity and any court, arbitrator or other tribunal); (iv) multi-national organization or body; or (v) individual, body or other entity exercising, or entitled to exercise, any executive, legislative, judicial, administrative, regulatory, police, military or taxing authority or power of any nature.

"In-Licenses" shall have the meaning ascribed to the term In-Licenses in Section 1.1.36 of the License Agreement.

"Indemnified Party" is defined in Section 8.2.

"Indemnifying Party" is defined in Section 8.2.

"Joint Invention" shall have the meaning ascribed to the term Joint Invention in Section 1.1.37 of the License Agreement.

"Joint Invention Patents" means all Patent Rights claiming or covering any Joint Inventions.

"Judgment" means any judgment, order, writ, injunction, citation, award or decree of any nature.

"KHK Inventions" shall have the meaning ascribed to the term KHK Inventions in Section 1.1.39 of the License Agreement.

"KHK Know-How" shall have the meaning ascribed to the term Licensed Know-How in Section 1.1.46 of the License Agreement.

"KHK Invention Patents" means all Patent Rights claiming or covering any KHK Inventions.

"KHK Patent Rights" shall have the meaning ascribed to the term Licensed Patent Rights in Section 1.1.47 of the License Agreement.

"Knowledge of the Seller" means the actual knowledge of the individuals listed on Schedule 1.1 of the Disclosure Schedule, after due inquiry.

"License Agreement" means that certain Collaboration and License Agreement, dated as of August 29, 2013, by and between the Seller and Licensee, as amended by that certain Amendment No. 1, dated as of August 24, 2015, that certain Amendment No. 2, dated as of November 28, 2016, Amendment No. 3, that certain Amendment No. 4, dated as of January 29, 2018, that certain Amendment No. 5, dated as of April 30, 2018, that certain Amendment No. 6, dated as of February 1, 2019, that certain Amendment No. 7, dated as of December 5, 2018, and that certain Amendment No. 8, dated as of July 4, 2019.

"Licensed KHK IP" means the KHK Patent Rights, the KHK Know-How, the KHK Inventions and Licensee's interest in the Joint Inventions.

"Licensed UGNX IP" means the UGNX Inventions and the Seller's interest in the Joint Inventions.

"Licensed IP" means, collectively, the Licensed KHK IP and the Licensed UGNX IP.

"Licensed Patents" is defined in Section 4.1(k)(i).

"Licensed Product" shall have the meaning ascribed to the term Licensed Product in Section 1.1.48 of the License Agreement.

"Licensee" means Kyowa Kirin Co. Ltd. (formerly, Kyowa Hakko Kirin Co., Ltd.) and any successor thereof, as permitted pursuant to the terms of this Agreement and the License Agreement.

"Licensee Consent" is defined in Section 3.5.

"Licensee Instruction Letter" is defined in Section 3.4.

"Lien" means any mortgage, lien, pledge, charge, adverse claim, security interest, encumbrance or restriction of any kind, including any restriction on use, transfer or exercise of any other attribute of ownership of any kind.

"Loss" means any and all Judgments, damages, losses, claims, costs, liabilities and expenses, including reasonable fees and out-of-pocket expenses of counsel.

"Material Adverse Effect" shall mean (i) a material adverse effect on the legality, validity or enforceability of any provision of this Agreement, (ii) a material adverse effect on the ability of the Seller to perform any of its obligations hereunder, (iii) a material adverse effect on the rights or remedies of the Buyer hereunder, (iv) a material adverse effect on the rights of the Seller under the License Agreement related to the Royalty or the European Territory or (v) an adverse effect on the timing, amount or duration of the payments to be made to the Buyer in respect of any portion of the Royalty or the right of the Buyer to receive such payments in any material respect (but excluding in each case any event, circumstance or change based on market conditions generally applicable to the industry in which the Seller operates or in any specific jurisdiction or geographical area, such as drug reimbursement rates or the commercial launch of a potentially competitive product).

"Mutually Agreed" means:

(a) for matters: (x) solely related to the Royalty or the European Territory, or (y) that would reasonably be expected (with or without the giving of notice or passage of time, or both) to result in a Material Adverse Effect, the Seller shall take (or refrain from taking) such reasonable actions in respect of each such matter as are reasonably requested by the Buyer;

(b) except with respect to matters related to routine intellectual property maintenance and prosecution, for matters under the License Agreement that: (x) do not relate to the Royalty or the European Territory and (y) would not reasonably be expected (with or without the giving of notice or passage of time, or both) to result in a Material Adverse Effect, the Seller shall have the right (subject to providing written notice to the Buyer) to take (or refrain from taking) such actions in respect of each such matter as the Seller, acting reasonably, deems appropriate; or

(c) except with respect to matters related to routine intellectual property maintenance and prosecution, for matters (x) involving a UGNX Invention Patent in the European Territory or a Joint Invention Patent (but subject to the extent of the Seller's rights under Section 10.2.1 of the License Agreement) in the European Territory, including patent term restoration, extension or adjustment, supplementary protection certificates and the like or any other similar foreign equivalent, or (y) all other matters under the License Agreement that (i) do not meet the criteria set forth in clauses (a) or (b) above), and (ii) would not reasonably be expected (with or without

the giving of notice or the passage of time, or both) to result in a Material Adverse Effect, the Seller shall take (or refrain from taking) actions in respect of each such matter as the Seller and the Buyer, each acting reasonably, mutually agree.

"Net Sales" shall have the meaning ascribed to the term Net Sales in Section 1.1.54 of the License Agreement.

"Opinion" is defined in Section 3.6.

"Patent Rights" shall have the meaning ascribed to the term Patent Rights in Section 1.1.58 of the License Agreement

"Permitted Liens" means any (i) mechanic's, materialmen's, and similar liens for amounts not yet due and payable, (ii) statutory liens for taxes not yet due and payable or for taxes that the taxpayer is contesting in good faith (iii) any liens in favor of, or granted to, Licensee pursuant to the License Agreement, (iv) any liens created, permitted or required by the Transaction Documents in favor of Buyer or its Affiliates, (v) Liens related to "march in" rights of the United States government under 35 U.S.C. §§ 200 – 212, and implementing regulations, and (iv) other liens and encumbrances not incurred in connection with the borrowing of money that do not materially and adversely affect the use or value of the affected assets provided that, in each case, such liens are automatically released upon the sale or other transfer of the affected assets (it being understood that any obligations secured by such "Permitted Liens" shall remain the obligations of the Seller).

"Person" means any individual, firm, corporation, company, partnership, limited liability company, trust, joint venture, association, estate, trust, Governmental Entity or other entity, enterprise, association or organization.

"Pharmacovigilance Agreement" means that certain Pharmacovigilance Agreement by and between [***] and Seller, dated as of December 20, 2017.

"Prime Rate" means the prime rate published by the Wall Street Journal, from time to time, as the prime rate.

"Proceeds" means any amounts actually recovered by the Seller as a result of any settlement or resolution of any actions, suits, proceedings, claims or disputes related to the License Agreement related to or involving the Royalty.

"Purchase Price" means $320,000,000.

"Representative" means, with respect to any Person, (i) any direct or indirect stockholder, member or partner of such Person and (ii) any manager, director, officer, employee, agent, advisor or other representative (including attorneys, accountants, consultants, bankers, financial advisors and actual and potential lenders and investors) of such Person.

"Royalty" means, on any date prior to the occurrence of the earlier of (a) the date on which aggregate payments of the Royalty owed to the Buyer equal the Royalty Cap or (b) the date of the last Royalty payment under the License Agreement, (i) all payments owed to Seller

under Section 7.2.1 of the License Agreement with respect to Net Sales of a Licensed Product in the European Territory from and after January 1, 2020, (ii) any payments to the Seller under the License Agreement in lieu of such payments of the foregoing clause (i), (iii) any payments to the Seller under Section 10.5.3(ii) of the License Agreement relating to a claim for Competing Product Infringement (as defined in the License Agreement) in the European Territory that occurred from and after January 1, 2020, (iv) any payments to the Seller under Section 15.5(c), (f) or (h) of the License Agreement with respect to the European Territory, and (v) any interest payments to the Seller under Section 7.4 of the License Agreement assessed on any payments described in the foregoing clauses (i), (ii), (iii) or (iv).

Notwithstanding the foregoing and for the avoidance of doubt, the term "Royalty" shall exclude: (i) any payments under Article 7 of the License Agreement, except those payments arising pursuant to Sections 7.2.1 and 7.4 described above, (ii) any damages or royalties payable to a Third Party under Section 10.6.3 of the License Agreement, (iii) reimbursements to Seller for costs and expenses incurred in connection with the preparation, filing, prosecution and maintenance of patent applications and patents in the KHK Patent Rights under Section 10.1.1 or the Joint Inventions under Section 10.2.1 of the License Agreement or litigation costs under Sections 10.5.3 or 10.6.1 of the License Agreement; (iv) any profit sharing payments and related cost reimbursements to Seller under Sections 7.1 and 7.2.2. of the License Agreement, or any milestone payments or upfront payments payable to Seller, if any, under Article 7 of the License Agreement, and (v) any indemnity payments to Seller and its Affiliates under Section 14.2 of the License Agreement that are not in respect of the Royalty.

"Royalty Cap" means either (a) if the aggregate payments of the Royalty in respect of Net Sales of Licensed Products made on or before December 31, 2030 and any other payments accrued prior to December 31, 2030 pursuant to clauses (ii) through (v) of the definition of "Royalty" are equal or greater than, in the aggregate, $608,000,000, then $608,000,000, or (b) if the payments of the Royalty in respect of Net Sales of Licensed Products made on or before December 31, 2030 actually received by the Buyer and any other payments actually received by the Buyer prior to December 31, 2030 pursuant to clauses (ii) through (v) of the definition of "Royalty" are, in the aggregate, less than $608,000,000, then $800,000,000.

"Royalty Reduction" is defined in Section 4.1(i)(xii).

"Royalty Reports" means the quarterly reports deliverable by Licensee pursuant to Section 7.2.4 of the License Agreement redacted to remove all information with respect to Licensed Products outside the European Territory.

"Royalty Termination Date" means the earlier of (a) the date on which aggregate payments of the Royalty actually received by the Buyer equal the Royalty Cap or (b) the date of the last Royalty payment under the License Agreement.

"Seller" is defined in the preamble.

"Seller Closing Certificate" is defined in Section 3.2(a).

"Seller Indemnified Parties" is defined in Section 8.1(b).

"Tax" or "Taxes" means any federal, state, local or non-U.S. income, gross receipts, license, payroll, employment, excise, severance, occupation, premium, windfall profits, environmental, customs duties, capital stock, franchise, profits, withholding, social security, unemployment, disability, real property, personal property, abandoned property, value added, alternative or add-on minimum, estimated or other tax of any kind whatsoever, including any interest, penalty or addition thereto, whether disputed or not.

"Third Party" shall have the meaning ascribed to the term Third Party in Section 1.1.77 of the License Agreement.

"Transaction Documents" means this Agreement, the Bill of Sale, the Disclosure Schedule, the Licensee Instruction Letter, and the Licensee Consent.

"UCC" means Article 9 of the New York Uniform Commercial Code, as in effect from time to time.

"UGNX Inventions" shall have the meaning ascribed to the term UGNX Inventions in Section 1.1.80 of the License Agreement.

"UGNX Invention Patents" means all Patent Rights claiming or covering any UGNX Inventions.

Certain Interpretations

. Except where expressly stated otherwise in this Agreement, the following rules of interpretation apply to this Agreement:

(a) "either" and "or" are not exclusive and "include," "includes" and "including" are not limiting and shall be deemed to be followed by the words "without limitation;"

(b) "extent" in the phrase "to the extent" means the degree to which a subject or other thing extends, and such phrase does not mean simply "if;"

(c) "hereof," "hereto," "herein" and "hereunder" and words of similar import when used in this Agreement refer to this Agreement as a whole and not to any particular provision of this Agreement;

(d) references to a Person are also to its permitted successors and assigns;

(e) definitions are applicable to the singular as well as the plural forms of such terms;

(f) unless otherwise indicated, references to an "Article", "Section" or "Exhibit" refer to an Article or Section of, or an Exhibit to, this Agreement, and references to a "Schedule" refer to the corresponding part of the Disclosure Schedule;

(g) references to "$" or otherwise to dollar amounts refer to the lawful currency of the United States; and

(h) references to a law include any amendment or modification to such law and any rules and regulations issued thereunder, whether such amendment or modification is made, or issuance of such rules and regulations occurs, before or after the date of this Agreement.

Headings

. The table of contents and the descriptive headings of the several Articles and Sections of this Agreement and the Exhibits and Schedules are for convenience only, do not constitute a part of this Agreement and shall not control or affect, in any way, the meaning or interpretation of this Agreement.

ARTICLE 2
PURCHASE, SALE AND ASSIGNMENT OF THE ROYALTY

Closing

; Purchase Price. Upon the terms and subject to the conditions of this Agreement, at the Closing, the Seller shall sell, transfer, assign and convey to the Buyer, and the Buyer shall purchase, acquire and accept from the Seller, free and clear of all Liens, all of the Seller's right, title and interest in and to the Royalty.

The purchase price to be paid to the Seller for the sale, transfer, assignment and conveyance of the Seller's right, title and interest in and to the Royalty to the Buyer is the Purchase Price, by wire transfer of immediately available funds to one or more accounts specified by the Seller on Exhibit A.

No Assumed Obligations, Etc

. Notwithstanding any provision in this Agreement to the contrary, the Buyer is purchasing, acquiring and accepting only the Royalty, and is not assuming any liability or obligation of the Seller of whatever nature, whether presently in existence or arising or asserted hereafter, under the License Agreement or otherwise. Except as specifically set forth herein in respect of the Royalty purchased, acquired and accepted hereunder, the Buyer does not, by such purchase, acquisition and acceptance, acquire any other contract rights of the Seller under the License Agreement or any other assets of the Seller.

True Sale

. It is the intention of the parties hereto that the sale, transfer, assignment and conveyance contemplated by this Agreement constitute a sale of the Royalty from the Seller to the Buyer and not a financing transaction, borrowing or loan. Accordingly, the Seller shall treat the sale, transfer, assignment and conveyance of the Royalty as a sale of an "account" or a "payment intangible" (as appropriate) in accordance with the UCC, and the Seller hereby authorizes the Buyer to file financing statements (and continuation statements with respect to such financing statements when applicable) naming the Seller as the debtor and the Buyer as the secured party in respect of the Royalty. Not in derogation of the foregoing statement of the intent of the parties hereto in this regard, and for the purposes of providing additional assurance to the Buyer in the event that, despite the intent of the parties hereto, the sale, transfer, assignment and conveyance contemplated hereby is hereafter held not to be a sale, the Seller does hereby grant to the Buyer, as security for the obligations of the Seller hereunder, a first priority security interest in and to all right, title and interest of the Seller, in, to and under the Royalty and any "proceeds" (as such term is defined in the UCC) thereof, and the Seller does hereby authorize the Buyer, from and after the Closing, to file such financing statements (and continuation statements with respect to such financing statements when applicable) as are necessary to perfect such security interest.

ARTICLE 3
CLOSING

Closings; Payment of Purchase Price.

(a) Closing. The purchase and sale of the Royalty shall take place on the date hereof, subject to the conditions set forth in Article 5 being satisfied, or at such other place, time and date as the parties hereto may mutually agree (the "Closing"). At the Closing, the Buyer shall deliver (or cause to be delivered) payment of the Purchase Price to the Seller by wire transfer of immediately available funds to one or more accounts specified by the Seller on Exhibit A.

Closing Certificates

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(a) Seller's Closing Certificate. At the Closing, the Seller shall deliver to the Buyer a certificate of the Secretary of the Seller, dated as of the Closing Date, certifying (i) as to the incumbency of the officer of the Seller executing this Agreement, (ii) as to the attached copies of Seller's certificate of incorporation, bylaws and resolutions adopted by the Seller's board of directors authorizing the execution and delivery by the Seller of this Agreement and the consummation by the Seller of the transactions contemplated hereby and (iii) that the conditions set forth in Section 5.1(a), Section 5.1(b) and Section 5.1(c) have been satisfied (the "Seller Closing Certificate").

(b) Buyer's Closing Certificate. At the Closing, RP Management LLC, as administrator of the Buyer, shall deliver to the Seller a certificate of an authorized person thereof, certifying that the conditions set forth in Section 5.2(a) and Section 5.2(b) have been satisfied (the "Buyer Closing Certificate").

(c) Buyer's Incumbency Certificate. At the Closing, the Buyer shall deliver to the Seller a certificate of an authorized person of the owner trustee of the Buyer certifying as to the incumbency of the officers executing this Agreement on behalf of Buyer (the "Buyer Incumbency Certificate").

Bill of Sale

. At the Closing, upon confirmation of the receipt of the Purchase Price, the Seller shall deliver to the Buyer a duly executed bill of sale evidencing the sale, transfer, assignment and conveyance of the Royalty, substantially in the form attached hereto as Exhibit B (the "Bill of Sale").

Licensee Instruction

. At the Closing, the Seller shall deliver to the Buyer an instruction letter, in substantially the form attached hereto as Exhibit C (the "Licensee Instruction Letter"), duly executed by the Seller, instructing Licensee to pay the Royalty to the account specified by the Buyer, which shall be delivered to the Licensee following the Closing.

Licensee Consent

. At Closing, the Seller shall deliver to the Buyer a consent letter, in substantially the form attached hereto as Exhibit D (the "Licensee Consent"), duly executed by the Seller and Licensee to be acknowledged by the Buyer, pursuant to which

Licensee (i) agrees that Seller may provide to the Buyer following the Closing copies of all Royalty Reports and all other notices, correspondence and confidential information relating to the Royalty or to the Licensed Products in the European Territory that are delivered by Licensee to the Seller pursuant to the terms of, or in respect of, the License Agreement, and (ii) agrees to pay the Royalty directly to the account in accordance with the Licensee Instruction Letter to be delivered to Licensee at the Closing.

Legal Opinion

. At the Closing, Gibson, Dunn & Crutcher LLP, as counsel to the Seller, shall deliver to the Buyer a duly executed legal opinion in the form previously agreed by the parties hereto (the "Opinion").

Form W-9

. At the Closing, the Seller shall deliver to the Buyer (a) a valid, properly executed IRS Form W-9 certifying that the Seller is exempt from U.S. federal withholding tax and "backup" withholding tax.

Form W-8BEN

-E. At the Closing, the Buyer shall deliver to the Seller a valid, properly executed IRS Form W-8BEN-E certifying that the Buyer is exempt from U.S. federal withholding tax with respect to any and all payments of in respect of the Royalty.

Data Room

. Within [***] days of the Closing, the Seller shall deliver to the Buyer an electronic copy of all of the information and documents posted to the virtual data room established by the Seller as of the date hereof and made available to the Buyer via Donnelley Financial Solutions' Venue Data Room (the "Data Room") for archival purposes only.

ARTICLE 4
REPRESENTATIONS AND WARRANTIES

Seller's Representations and Warranties

. Except as set forth in the Disclosure Schedule, the Seller represents and warrants to the Buyer that as of the date hereof:

Existence; Good Standing

. The Seller is a corporation duly incorporated, validly existing and in good standing under the laws of Delaware. The Seller is duly licensed or qualified to do business and is in corporate good standing in each jurisdiction in which the nature of the business conducted by it or the character or location of the properties and assets owned, leased or operated by it makes such licensing or qualification necessary, except where the failure to be so licensed or qualified and in corporate good standing has not and would not reasonably be expected to have, either individually or in the aggregate, a Material Adverse Effect.

Authorization

. The Seller has all requisite corporate power and authority to execute, deliver and perform its obligations under this Agreement. The execution, delivery and performance of this Agreement, and the consummation of the transactions contemplated hereby, have been duly authorized by all necessary corporate action on the part of the Seller.

Enforceability

. The Agreement has been duly executed and delivered and constitutes a valid and binding obligation of the Seller enforceable against the Seller in

accordance with its terms, except as such enforceability may be limited by applicable bankruptcy, securities, insolvency, or similar laws relating to, or affecting generally the enforcement of, creditors' rights and remedies, or indemnification or by other equitable principles of general application.

No Conflicts

. The execution, delivery and performance by the Seller of this Agreement and the consummation of the transactions contemplated hereby do not and shall not (i) contravene or conflict with the organizational documents of the Seller, (ii) contravene or conflict with or constitute a material default under any law or Judgment binding upon or applicable to the Seller, (iii) contravene or conflict with or constitute a default under the License Agreement or (iv) contravene or conflict with or constitute a material default under any other material contract or material agreement binding upon or applicable to the Seller.

Consents

. Except for the Licensee Consent and the consents that have been obtained on or prior to the Closing or filings required by the federal securities laws or stock exchange rules, no consent, approval, license, order, authorization, registration, declaration or filing with or of any Governmental Entity or other Person is required to be done or obtained by the Seller in connection with (i) the execution and delivery by the Seller of this Agreement, (ii) the performance by the Seller of its obligations under this Agreement or (iii) the consummation by the Seller of any of the transactions contemplated by this Agreement.

No Litigation

. There is no action, suit, investigation or proceeding pending before any Governmental Entity or, to the Knowledge of the Seller, threatened to which the Seller is a party that, individually or in the aggregate would, if determined adversely, reasonably be expected to have a Material Adverse Effect.

Compliance with Laws

. The Seller is not in violation of, and to the Knowledge of the Seller, the Seller is not under investigation with respect to nor has the Seller been threatened to be charged with or given notice of any violation of, any law or Judgment applicable to the Seller, which violation would reasonably be expected to have a Material Adverse Effect.

No Undisclosed Events or Circumstances

. Except for the transactions contemplated hereby, no event or circumstance has occurred or exists with respect to the Seller, its Affiliates, or their respective businesses, properties, operations or financial condition, which, under applicable law, rule or regulation, requires public disclosure or announcement by the Seller but which has not been so publicly announced or disclosed and which, individually or in the aggregate, would constitute a Material Adverse Effect. There is no action, suit, claim, investigation or proceeding pending or, to the Knowledge of the Seller, threatened against the Seller or any of its Affiliate which questions the validity of this Agreement or the transactions contemplated hereby or any action taken or to be taken pursuant hereto. There is no action, suit, claim, investigation or proceeding pending or, to the Knowledge of the Seller, threatened, against or involving the Seller or any of its Affiliates, or any of their respective properties or assets that would be reasonably be expected to result in a Material Adverse Effect.

License Agreement

. Attached hereto as Exhibits E-1, E-2, and E-3 are true, correct and complete copies of, respectively, the License Agreement, the

Pharmacovigilance Agreement, and the Distribution Agreement. The Seller has delivered to the Buyer true, correct and complete copies of (A) all material communications between the Seller and Licensee since February 1, 2017 relating to the Royalty or to the Licensed Products in the European Territory, (B) all Royalty Reports provided to the Seller by Licensee as of the Closing Date pursuant to Section 7.2.4 of the License Agreement, and (C) all minutes from and meeting materials of the JSC (as such term is defined in the License Agreement) since February 1, 2017, related to the Royalty or the Licensed Products in the European Territory, and redacted to reflect solely such information.

(i) No Other Agreements. Except as set forth on Schedule 4.1(i)(i)(A) of the Disclosure Schedule, the License Agreement, the Pharmacovigilance Agreement, and the Distribution Agreement are the only agreements, instruments, arrangements, waivers or understandings (collectively, "Contracts") between the Seller (or any predecessor or Affiliate thereof), on the one hand, and Licensee (or any predecessor or Affiliate thereof), on the other hand, relating to the subject matter thereof, and there are no other Contracts between the Seller (or any predecessor or any Affiliate thereof), on the one hand, and Licensee (or any predecessor or Affiliate thereof), on the other hand, that relate to the License Agreement, the Licensed IP, the Licensed Products (including the development or commercialization thereof), or the Royalty. Except as set forth on Schedule 4.1(i)(i)(B) of the Disclosure Schedule, the Seller has not proposed or received any proposal, to amend or waive any provision of (1) the License Agreement since July 4, 2019, or (2) any of the Pharmacovigilance Agreement or the Distribution Agreement in each case of clause (1) and (2) in any manner that (x) would result in a breach of this Agreement or (y) would otherwise reasonably be expected (with or without the giving of notice or the passage of time, or both) to have a Material Adverse Effect. None of the executed Contracts and none of the draft Contracts in the form each exists as of the date hereof, and in each case as listed on Schedule 4.1(i)(i)(A) of the Disclosure Schedule, contain any provision, term or condition that would reasonably be expected to result in a Material Adverse Effect. The draft Contract in the form it exists as of the date hereof and listed on Schedule 4.1(i)(i)(B)(x) of the Disclosure Schedule does not contain any provision, term or condition that would reasonably be expected to result in a Material Adverse Effect.

(ii) Licenses/Sublicenses. Except as set forth on Schedule 4.1(i)(ii) of the Disclosure Schedule, to the Knowledge of the Seller, there are no licenses or sublicenses entered into by Licensee or any other Person (or any predecessor or Affiliate thereof) in respect of Licensee's rights and obligations under the License Agreement (including any Licensed IP) related to the European Territory. The Seller has not received any notice from Licensee pursuant to Section 2.7.1 or Section 13.1.1 of the License Agreement.

(iii) Validity and Enforceability of License Agreement. The License Agreement is legal, valid, binding, enforceable, and in full force and effect. The License Agreement will continue to be legal, valid, binding, enforceable, and in full force and effect on identical terms except for such terms

modified as expressly set forth in the Licensee Consent and the Licensee Instruction Letter, immediately following the consummation of the transactions contemplated by this Agreement. No party to the License Agreement is in material, substantial and ongoing breach thereof, and no event has occurred that with notice or lapse of time would constitute such a breach, or permit termination, modification, or acceleration, under the License Agreement. No party to the License Agreement has repudiated any provision of the License Agreement and the Seller has not received any notice in connection with the License Agreement challenging the validity, enforceability or interpretation of any provision of such agreement, including the obligation to pay any portion of the Royalty without set-off of any kind.

(iv) Licensed Product. Burosumab is a Drug Substance and is the active ingredient in the Licensed Products. Licensee and its Affiliates are required to pay royalties under Section 7.2.1 of the License Agreement on all Net Sales by or on behalf of them and any of their (sub)licensees of any Licensed Products in the Field in the European Territory. The Seller has the right to receive the Royalty on Net Sales of the Licensed Products in the Field in the European Territory for so long as Licensee, one of its Affiliates or any of its or their (sub)licensees is selling the Licensed Products in any country in the European Territory.

(v) No Liens or Assignments by the Seller. The Seller has not, except for Permitted Liens and as contemplated hereby, conveyed, assigned or in any other way transferred or granted any liens upon or security interests with respect to all or any portion of its right, title and interest in and to the Royalty, Seller's interest in the Joint Invention Patents or the License Agreement.

(vi) No Waivers or Releases. The Seller has not granted any material waiver under the License Agreement with respect to the Royalty or the European Territory and has not released Licensee, in whole or in part, from any of its material obligations with respect to the Royalty or the European Territory under the License Agreement.

(vii) No Termination. The Seller has not (A) given Licensee any notice of termination of the License Agreement (whether in whole or in part) or any notice expressing any intention to terminate the License Agreement or (B) received any notice of termination of the License Agreement (whether in whole or in part) or any notice expressing any intention to terminate either the License Agreement. To the Knowledge of the Seller, no event has occurred that would give rise to the expiration or termination of the License Agreement.

(viii) No Breaches or Defaults. There is and has been no material breach or default under any provision of the License Agreement either by the Seller (or any predecessor thereof) or, to the Knowledge of the Seller, by Licensee (or any predecessor thereof), and there is no event that upon notice or the passage of time, or both, would reasonably be expected to give rise to any

material breach or default either by the Seller or, to the Knowledge of the Seller, by Licensee.

(ix) Payments Made. The Seller has received from Licensee (including from one or more Affiliates of Licensee in accordance with Section 13.6 of the License Agreement) the full amount of the payments due and payable under the License Agreement.

(x) No Assignments by Licensee. The Seller has not consented to any assignment, delegation or other transfer by Licensee or any of its predecessors of any of their rights or obligations under the License Agreement with respect to the European Territory, and, to the Knowledge of the Seller, Licensee has not assigned or otherwise transferred or granted any liens upon or security interest with respect to any of its rights or obligations under the License Agreement with respect to the European Territory or, to the Knowledge of the Seller, any portion of its right, title and interest in and to the Licensed KHK IP with respect to the European Territory, in each case, to any Person.

(xi) No Indemnification Claims. The Seller has not notified Licensee or any other Person of any claims for indemnification under the License Agreement nor has the Seller received any claims for indemnification under the License Agreement pursuant to Article 14 thereof.

(xii) No Royalty Reductions. To the Knowledge of the Seller, the amount of the Royalty, due and payable under Section 7.2.1 of the License Agreement, as of the date hereof, is not subject to any claim by Licensee alleging a right of set-off, counterclaim, credit, reduction or deduction by contract or otherwise against such Royalty, including in respect of any royalties payable by the Seller to Licensee pursuant to Section 7.2.3 of the License Agreement (each, a "Royalty Reduction"). To the Knowledge of the Seller, no event or condition exists that, upon notice or passage of time or both, would reasonably be expected to permit Licensee to claim, or have the right to claim, a Royalty Reduction.

(xiii) No Notice of Infringement. The Seller has not received any written notice from, or given any written notice to, Licensee pursuant to Sections 10.5.1 or 10.6.3 of the License Agreement.

(xiv) Audits. The Seller has not initiated, pursuant to Section 9.2 of the License Agreement any inspection or audit of books of accounts or other records pertaining to Net Sales, the calculation of royalties or other amounts payable to the Seller under the License Agreement.

(xv) In-Licenses. To the Knowledge of the Seller, and with respect to each agreement constituting an In-License, (A) such agreement is valid and in full force and effect, and binding and enforceable on Licensee and its counterparty, (B) Licensee has not given the counterparty to any such agreement any notice of termination or any notice expressing an intention to terminate such

agreement, and Licensee has not received the same from such counterparty, (C) there is no and has been no material breach under any provision of such agreement by Licensee or its counterparty, and (D) Licensee has not proposed, or received any proposal, to amend or waive any provision of such agreement in a manner that would reasonably be expected to result in a Material Adverse Effect.

Title to Royalty

. The Seller has good and marketable title to the Royalty free and clear of all Liens (other than Permitted Liens). Upon payment of the Purchase Price by the Buyer, the Buyer will acquire, subject to the terms and conditions set forth in this Agreement and the License Agreement, good and marketable title to the Royalty, free and clear of all Liens (other than Permitted Liens and Liens created by the Buyer).

Intellectual Property

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(i) Schedule 4.1(k)(i) of the Disclosure Schedule lists all Joint Invention Patents and KHK Patent Rights (collectively, the "Licensed Patents"). To the Knowledge of the Seller, Licensee is the sole owner of, or is in possession of a valid license to, all of the KHK Patent Rights. The Seller and Licensee collectively are the sole owners of, and collectively have the sole interest in, the Joint Invention Patents, and the Seller is the sole owner of, and has sole interest in, its undivided half interest in each of the Joint Invention Patents. Schedule 4.1(l)(i) of the Disclosure Schedule specifies as to each of the Licensed Patents, as applicable, the jurisdictions by or in which each such patent has issued as a patent or such patent application has been filed, including the respective patent numbers and application numbers and issue and filing dates. Neither Seller nor any of its Affiliates owns any Patent Rights that are UGNX Invention Patents, and, to the Knowledge of the Seller, neither KHK nor any of its Affiliates owns any Patent Rights that are KHK Invention Patents.

(ii) Except as set forth in Schedule 4.1(k)(ii) of the Disclosure Schedule, there are no pending or, to the Knowledge of the Seller, threatened litigations, interferences, reexamination, oppositions or like procedures involving any Joint Invention Patent. To the Knowledge of the Seller, there are no pending or threatened litigations, interferences, reexamination, oppositions or the like procedures involving any KHK Patent Right.

(iii) All of the issued Joint Invention Patents are in full force and effect and have not lapsed, expired or otherwise terminated, and, to the Knowledge of the Seller, are valid and enforceable. The Seller has not received any written notice relating to the lapse, expiration or other termination of any of the Joint Invention Patents, or any written legal opinion that alleges that any of the issued Joint Invention Patents is invalid or unenforceable. To the Knowledge of the Seller, all of the issued KHK Patent Rights are in full force and effect and have not lapsed, expired or otherwise terminated, and are valid and enforceable.

(iv) To the Knowledge of the Seller, there is no Person who is or claims to be an inventor under any of the Joint Invention Patents who is not a named inventor thereof.

(v) The Seller has not, and, to the Knowledge of the Seller, Licensee has not, received any written notice of any claim by any Person challenging the inventorship or ownership of, the rights of the Seller or Licensee, as applicable, in and to, or the patentability, validity or enforceability of, any Licensed Patent, or asserting that the development, manufacture, importation, sale, offer for sale or use of any Licensed Product infringes any patent or other intellectual property rights of such Person.

(vi) To the Knowledge of the Seller, the discovery and development of the Licensed Products did not and does not infringe, misappropriate or otherwise violate any patent rights or other intellectual property rights owned by any third party. Neither the Seller nor, to the Knowledge of the Seller, Licensee, has, except pursuant to the In-Licenses, and except for two patent families added to the KHK Patent Rights in Amendment No. 3, in-licensed any patents or other intellectual property rights covering the manufacture, use, sale, offer for sale or import of the Licensed Products.

(vii) To the Knowledge of the Seller, the manufacture, use, marketing, sale, offer for sale, importation or distribution of the Licensed Products has not and will not, infringe, misappropriate or otherwise violate any patent rights or other intellectual property rights owned by any other Person.

(viii) To the Knowledge of the Seller, no third party has infringed, misappropriated or otherwise violated, or is infringing, misappropriating or otherwise violating, any of the Licensed Patents.

(ix) All required maintenance fees, annuities and like payments with respect to the Licensed Patents for which the Seller controls the prosecution and maintenance in accordance with Section 10.1.1 or 10.2.1 of the License Agreement, and to the Knowledge of the Seller, with respect to all other Licensed Patents, have been paid timely.

UCC Representation and Warranties

. The Seller's exact legal name is, and for the immediately preceding ten years has been, "Ultragenyx Pharmaceutical Inc.". Seller is, and for the prior eight years has been, incorporated in Delaware.

Brokers' Fees

. Other than Perella Weinberg Partners LP and J. Wood Capital Advisors, LLC, there is no investment banker, broker, finder, financial advisor or other intermediary who has been retained by or is authorized to act on behalf of the Seller who might be entitled to any fee or commission in connection with the transactions contemplated by this Agreement.

The Buyer's Representations and Warranties

. The Buyer represents and warrants to the Seller that as of the date hereof:

(a) Existence; Good Standing. The Buyer is a statutory trust duly organized, validly existing and in good standing under the laws of the State of Delaware.

(b) Authorization. The Buyer has the requisite trust right, power and authority to execute, deliver and perform its obligations under this Agreement. The execution, delivery and performance of this Agreement, and the consummation of the transactions contemplated hereby, have been duly authorized by all necessary action on the part of the Buyer.

(c) Enforceability. This Agreement has been duly executed and delivered by an authorized person of the owner trustee of the Buyer and constitutes the valid and binding obligation of the Buyer, enforceable against the Buyer in accordance with its terms, except as may be limited by applicable Bankruptcy Laws or by general principles of equity (whether considered in a proceeding in equity or at law).

(d) No Conflicts. The execution, delivery and performance by the Buyer of this Agreement do not and shall not (i) contravene or conflict with the organizational documents of the Buyer, (ii) contravene or conflict with or constitute a default under any material provision of any law binding upon or applicable to the Buyer or (iii) contravene or conflict with or constitute a default under any material contract or other material agreement or Judgment binding upon or applicable to the Buyer.

(e) Consents. No consent, approval, license, order, authorization, registration, declaration or filing with or of any Governmental Entity or other Person is required to be done or obtained by the Buyer in connection with (i) the execution and delivery by the Buyer of this Agreement, (ii) the performance by the Buyer of its obligations under this Agreement, other than the filing of financing statement(s) in accordance with Section 2.3, or (iii) the consummation by the Buyer of any of the transactions contemplated by this Agreement.

(f) No Litigation. There is no action, suit, investigation or proceeding pending or, to the knowledge of the Buyer, threatened before any Governmental Entity to which the Buyer is a party that would, if determined adversely, reasonably be expected to prevent or materially and adversely affect the ability of the Buyer to perform its obligations under this Agreement.

(g) Financing. The Buyer has sufficient cash on hand to pay the entire Purchase Price. The Buyer acknowledges that its obligations under this Agreement are not contingent on obtaining financing.

(h) Brokers' Fees. There is no investment banker, broker, finder, financial advisor or other intermediary who has been retained by or is authorized to act on behalf of the Buyer who might be entitled to any fee or commission in connection with the transactions contemplated by this Agreement.

No Implied Representations and Warranties

. EXCEPT AS EXPRESSLY SET FORTH IN SECTION 4.1, THE SELLER MAKES NO REPRESENTATION OR WARRANTY, EXPRESSED OR IMPLIED, AT LAW OR IN EQUITY, INCLUDING WITH RESPECT TO MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE, AND ANY SUCH REPRESENTATIONS OR

WARRANTIES ARE HEREBY EXPRESSLY DISCLAIMED. BUYER ACKNOWLEDGES THAT, EXCEPT AS SPECIFICALLY PROVIDED IN THIS ARTICLE 4 AND THE DISCLOSURE SCHEDULES, SELLER HAS ASSUMED NO RESPONSIBILITIES OF ANY KIND WITH RESPECT TO ANY ACT OR OMISSION OF LICENSEE WITH RESPECT TO THE DESIGN, DEVELOPMENT, MANUFACTURE, USE, SALE, DISTRIBUTION, MARKETING OR OTHER ACTIVITIES OF LICENSEE WITH RESPECT TO ANY OF THE THE LICENSED PRODUCTS.

ARTICLE 5
CONDITIONS TO CLOSING

Conditions to the Buyer's Obligations

. The obligations of the Buyer to consummate the transactions contemplated hereunder on the Closing Date are subject to the satisfaction or waiver, at or prior to the Closing Date, of each of the following conditions precedent.

(a) The Seller shall have performed and complied in all material respects with all, and shall not be in material breach of any, agreements, covenants, obligations and conditions required to be performed and complied by it under this Agreement at or prior to the Closing Date.

(b) The representations and warranties of the Seller contained in Article 3 shall be true and correct in all material respects as of the Closing Date as though made at and as of the Closing Date, except to the extent any such representation or warranty expressly speaks as of a particular date, in which case it shall be true and correct in all material respects as of such date; provided, that to the extent that any such representation or warranty is qualified by the term "material" or "Material Adverse Effect," such representation or warranty (as so written, including the term "material" or "Material Adverse Effect") shall be true and correct in all respects as of the Closing Date or such other date, as applicable.

(c) After the date of this Agreement, there shall not have occurred any fact, circumstance, effect, change, event or development that, individually or in the aggregate, has resulted, or would reasonably be likely to result, in a Material Adverse Effect.

(d) There shall not have been issued and be in effect any Judgment of any Governmental Entity enjoining, preventing or restricting the consummation of the transactions contemplated by this Agreement.

(e) There shall not have been instituted or be pending any action or proceeding by any Governmental Entity or any other Person (i) challenging or seeking to make illegal, to delay materially or otherwise directly or indirectly to restrain or prohibit the consummation of the transactions contemplated hereby, (ii) seeking to obtain material damages in connection with the transactions contemplated hereby or (iii) seeking to restrain or prohibit the Buyer's receipt of the Royalty.

(f) The Seller shall have delivered to the Buyer the duly executed Bill of Sale.

(g) The Seller shall have delivered to the Buyer the duly executed Licensee Consent.

(h) The Seller shall have delivered to the Licensee and the Buyer the duly executed Licensee Instruction Letter for the Buyer to deliver to Licensee following the Closing.

(i) The Seller shall have delivered to the Buyer the duly executed Opinion.

(j) The Seller shall have delivered to the Buyer the duly executed Seller Closing Certificate.

Conditions to the Seller's Obligations

. The obligations of the Seller to consummate the transactions contemplated hereunder on the Closing Date are subject to the satisfaction or waiver, at or prior to the Closing Date, of each of the following conditions precedent:

(a) The Buyer shall have performed and complied in all material respects with all, and shall not be in material breach of any, agreements, covenants, obligations and conditions required to be performed and complied by it under this Agreement at or prior to the Closing Date.

(b) The representations and warranties of the Buyer contained in Section 4.2 shall be true and correct in all material respects as of the Closing Date as though made at and as of the Closing Date, except to the extent any such representation or warranty expressly speaks as of a particular date, in which case it shall be true and correct in all material respects as of such date; provided, that to the extent that any such representation or warranty is qualified by the term "material," such representation or warranty (as so written, including the term "material") shall be true and correct in all respects as of the Closing Date or such other date, as applicable.

(c) There shall not have been issued and be in effect any Judgment of any Governmental Entity enjoining, preventing or restricting the consummation of the transactions contemplated by this Agreement.

(d) There shall not have been instituted or be pending any action or proceeding by any Governmental Entity or any other Person (i) challenging or seeking to make illegal, to delay materially or otherwise directly or indirectly to restrain or prohibit the consummation of the transactions contemplated hereby, (ii) seeking to obtain material damages in connection with the transactions contemplated hereby or (iii) seeking to restrain or prohibit the Buyer's receipt of the Royalty.

(e) The Buyer shall have delivered to the Seller the duly executed Buyer Closing Certificate.

(f) The Buyer shall have delivered to the Seller the duly executed Buyer Incumbency Certificate.

ARTICLE 6
COVENANTS

Disclosures

. Except for a press release previously approved in form and substance by the Seller and the Buyer or any other public announcement using substantially the same text as such press release, neither the Buyer nor the Seller shall, and each party hereto shall cause its respective Representatives, Affiliates and Affiliates' Representatives not to, issue a press release or other public announcement or otherwise make any public disclosure with respect to this Agreement or the subject matter hereof without the prior written consent of the other party hereto (which consent shall not be unreasonably withheld, conditioned or delayed), except as may be required by applicable law or stock exchange rule (in which case the party hereto required to make the press release or other public announcement or disclosure shall allow the other party hereto reasonable time to comment on such press release or other public announcement or disclosure in advance of such issuance).

Payments Received In Error; Interest

.

(a) Commencing on the Closing Date and until the Royalty Termination Date, if any payment of any portion of the Royalty is made to the Seller, the Seller shall pay such amount to the Buyer, promptly (and in any event within [***] Business Days) after the receipt thereof, by wire transfer of immediately available funds to an account designated in writing by the Buyer. The Seller shall notify the Buyer of such wire transfer and provide reasonable details regarding the Royalty payment so received by the Seller. The Seller agrees that, in the event any payment of the Royalty is paid to the Seller, the Seller shall (i) until paid to the Buyer, hold such payment received in trust for the benefit of the Buyer and (ii) have no right, title or interest in such payment and that it shall not pledge or otherwise grant any security interest therein.

(b) Commencing on the Closing Date and at all times thereafter if any payment due under the License Agreement that does not constitute the Royalty is made to the Buyer, the Buyer shall pay such amount to the Seller, promptly (and in any event within [***] Business Days) after the receipt thereof, by wire transfer of immediately available funds to an account designated in writing by the Seller. The Buyer shall notify the Seller of such wire transfer and provide reasonable details regarding the erroneous payment so received by the Buyer. The Buyer agrees that, in the event any payment due under the License Agreement that does not constitute the Royalty is paid to the Buyer, the Buyer shall (i) until paid to the Seller, hold such payment received in trust for the benefit of the Seller and (ii) have no right, title or interest in such payment and that it shall not pledge or otherwise grant any security interest therein.

(c) A late fee of [***] shall accrue on all unpaid amounts on an annualized basis with respect to any sum payable under Section 6.2(a) beginning [***] Business Days, or under Section 6.2(b) beginning [***] Business Days, after receipt of such payment received in error.

Royalty Reduction

. If Licensee exercises any Royalty Reduction against any payment of the Royalty, such Royalty Reduction shall not reduce any payment of the

Royalty otherwise payable to the Buyer, and if such Royalty Reduction reduces any payment of the Royalty to less than the full amount of the Royalty, then Seller shall promptly (and in any event within [***] Business Days following the payment of the Royalty affected by such Royalty Reduction) make a true-up payment to the Buyer such that the Buyer receives the full amount of such Royalty payments that would have been payable to the Buyer had such Royalty Reduction not occurred.

Royalty Reports; Notices and Other Information from the Licensee

. Promptly (and in any event within [***] Business Days) following the receipt by the Seller of any Royalty Report or other material notices or correspondence relating to the Royalty or the Licensed Product in the European Territory that has been provided to the Seller under, or in respect of, the License Agreement, the Seller shall furnish a true, correct and complete copy of the same to the Buyer.

Notices and Other Information to the Licensee

. The Seller shall not send (or refrain from sending), without the prior written consent of the Buyer, any material written notice or correspondence to Licensee that (a) relates to the Royalty or the European Territory or (b) would, or relates to a matter that would, reasonably be expected (with or without the giving of notice or passage of time, or both) to result in a Material Adverse Effect.

Inspections and Audits of Licensee

. At the written request of the Buyer upon not less than [***] days' prior written notice, the Seller shall, to the extent permitted under Section 9.2.1 of the License Agreement, provide written notice to Licensee to cause an inspection or audit during normal business hours not more than [***] each calendar year, and under a customary non-disclosure agreement, by an independent public accounting firm to be made for the purpose of determining the correctness of Royalty payments made under the License Agreement. With respect to any inspection or audit requested by the Buyer with respect to the Royalty, the Seller shall, for purposes of Section 9.2.1 of the License Agreement, select such independent public accounting firm as the Buyer shall recommend for such purpose (as long as such independent certified public accountant is reasonably acceptable to Licensee as required by Section 9.2.1 of the License Agreement). The Buyer shall pay the Seller the expenses of any inspection or audit requested by the Buyer (including the fees and expenses of such independent public accounting firm designated for such purpose) that would otherwise be borne by the Seller pursuant to the License Agreement (if and as such expenses are actually incurred by the Seller). The Seller shall deliver to the Buyer a copy of the results of any audit conducted pursuant to Section 9.2.1 of the License Agreement within [***] Business Days following the Seller's receipt thereof, with information redacted that the Seller reasonably determines is not relevant for determining the correctness of Royalty payments made under the License Agreement.

Amendment or Assignment of License Agreement

. The Seller shall not, except as Mutually Agreed, assign, amend, modify, supplement or restate (or consent to any assignment, amendment, modification, supplement or restatement of) any provision of the License Agreement. Subject to the foregoing, promptly, and in any event within [***] Business Days, following receipt by the Seller of any final assignment, amendment, modification, supplement or restatement of the License Agreement, the Seller shall furnish a copy of the same to the Buyer.

Maintenance of License Agreement

. The Seller shall comply in all material respects with its obligations under the License Agreement and shall not take any action or forego any action that would reasonably be expected to constitute a material breach or default thereof. Promptly, and in any event within [***] Business Days, after receipt of any (written or oral) notice from Licensee of an alleged breach or default under the License Agreement relating to the Royalty or to the Licensed Products in the European Territory or of other material breach by the Seller under the License Agreement, the Seller shall give notice thereof to the Buyer, including delivering the Buyer a copy of any such written notice. After consultation with the Buyer and as Mutually Agreed, the Seller shall use its reasonable best efforts to cure any such breach or default by it under the License Agreement and shall give written notice to the Buyer upon curing any such breach or default. In connection with any dispute regarding an alleged breach that is solely related to the Royalty or could reasonably be expected (with or without the giving of notice or passage of time, or both) to have a Material Adverse Effect, the Seller shall employ such counsel, reasonably acceptable to the Seller, as the Buyer may select. The Buyer shall pay the costs and expenses of such counsel in connection with any dispute regarding any such breach by the Licensee, and the Seller shall pay the costs and expenses of such counsel in connection with any dispute regarding any such breach by Seller. The Seller shall not, except as Mutually Agreed, (a) forgive, release or compromise any amount owed to or becoming owed to the Seller under the License Agreement in respect of the Royalty or (b) waive any obligation of, or grant any consent to, the Licensee under, in respect of or related to the Royalty. The Seller shall not exercise or enforce its applicable rights under the License Agreement in any manner that would reasonably be expected (with or without the giving of notice or the passage of time, or both) to have a Material Adverse Effect.

Enforcement of License Agreement

.

(a) Notice of Breaches by Licensee. Promptly (and in any event within [***] Business Days) after the Seller becomes aware of, or comes to believe in good faith that there has been a material breach of the License Agreement by Licensee, the Seller shall provide notice of such breach to the Buyer. In addition, the Seller shall provide to the Buyer a copy of any written notice of such breach or alleged breach of the License Agreement delivered by the Seller to Licensee as soon as practicable and in any event not less than [***] Business Days following such delivery.

(b) Enforcement of License Agreement. In the case of any material breach by Licensee referred to in Section 6.9(a), the Seller shall consult with the Buyer regarding the timing, manner and conduct of any enforcement of Licensee's obligations under the License Agreement. Following such consultation, the Seller shall, (i) as Mutually Agreed, exercise such rights and remedies relating to any such breach as shall be available to Seller, whether under the License Agreement or by operation of law and, (ii) if such breach is solely related to the Royalty or could reasonably be expected (with or without the giving of notice or passage of time, or both) to have a Material Adverse Effect, employ such counsel reasonably acceptable to the Seller as the Buyer shall recommend for such purpose.

(c) Allocation of Proceeds and Costs of Enforcement. Each of the Buyer and the Seller shall bear its own fees and expenses incurred in enforcing Licensee's obligations under the License Agreement pursuant to this Section 6.9, provided that the Buyer shall pay the costs

and expenses of any counsel employed by the Seller pursuant to Section 6.9(b)(ii). The Proceeds resulting from any enforcement of Licensee's obligations under the License Agreement undertaken at the Buyer's request pursuant to this Section 6.9 shall be applied first to reimburse the Seller and the Buyer for any expenses incurred by them in connection with such enforcement (including notwithstanding the occurrence of the Royalty Termination Date), with the remainder of the Proceeds distributed to (i) the Buyer if the breach by Licensee is solely related to the Royalty or (ii) the Seller for all other breaches by Licensee. The Seller hereby assigns and, if not presently assignable, agrees to assign to the Buyer the amount of Proceeds due to the Buyer in accordance with this Section 6.9.

Termination of License Agreement

. The Seller shall not, without the prior written consent of the Buyer, (i) exercise any right to terminate the License Agreement, in whole or in part (but only if termination of such part could reasonably be expected (with or without the giving of notice or passage of time, or both) to have a Material Adverse Effect), (ii) agree with Licensee to terminate the License Agreement, in whole or in part (but only if termination of such part could reasonably be expected (with or without the giving of notice or passage of time, or both) to have a Material Adverse Effect), or (iii) take, or permit any Affiliate or sublicensee to take, any action that would reasonably be expected to give Licensee the right to terminate the License Agreement, in whole or in part (but only if termination of such part could reasonably be expected (with or without the giving of notice or passage of time, or both) to have a Material Adverse Effect). The Seller shall not take any action, fail to take an action or permit an action to be taken, that would give Licensee the right to terminate the License Agreement under Section 15.2.1 or 15.2.2 thereof or Section 4 of Amendment No. 3.

Preservation of Rights

. The Seller shall not, except as Mutually Agreed, hereafter sell, transfer, hypothecate, assign or in any manner convey or mortgage, pledge or grant a security interest or other encumbrance of any kind in any of its interest in any portion of the License Agreement or any of its interest in the Joint Invention Patents that could reasonably be expected (with or without the giving of notice or passage of time, or both) to have a Material Adverse Effect. The Seller shall not hereafter subject to a Lien (other than a Permitted Lien), sell, transfer, assign, convey title (in whole or in part), grant any right to, or otherwise dispose of any portion of the Royalty.

Enforcement; Defense; Prosecution and Maintenance

.

(a) The Buyer and Seller shall promptly inform each other of any suspected infringement by a third party they become aware of in the European Territory with respect to any of the Licensed Patents or any other patent right claiming the composition of matter of, or the method of making or using, any Licensed Product in the European Territory. The Seller shall (i) provide to the Buyer a copy of any written notice of any suspected infringement in the European Territory of any of the Licensed Patents and all pleadings filed in such action and (ii) notify the Buyer of any material developments in any claim, suit or proceeding resulting from such infringement that are delivered by Licensee to the Seller under Section 10.5.1 of the License Agreement or otherwise as soon as practicable and in any event not less than [***] Business Days following such delivery.

(b) If the Seller has the right to join an enforcement action in the European Territory as set forth in Section 10.5.1 of the License Agreement, the Seller shall, if requested in writing by the Buyer, promptly, and in any event within [***] Business Days after receipt of such request, exercise such right as instructed by the Buyer and, if requested by the Buyer, the Seller shall employ such counsel reasonably acceptable to the Seller as the Buyer shall recommend for such purpose, provided that the Buyer shall pay the costs and expenses of any such counsel. The Seller shall not join any infringement action in the European Territory under Section 10.5.1 of the License Agreement without the Buyer's prior consent.

(c) Promptly (and in any event within [***] Business Days) following the Seller receiving written notice from the Licensee pursuant to Section 10.1.1 of the License Agreement or, if applicable where Licensee was appointed the lead-party, Section 10.2.1 of the License Agreement, of the Licensee's intention to allow any of the KHK Patent Rights in the European Territory or the Joint Invention Patents in the European Territory to lapse or become abandoned or to not file patent applications for any of the KHK Patent Rights in the European Territory or Joint Invention Patents in the European Territory (such Patent Rights, the "Applicable Patents"), the Seller shall inform the Buyer of such notice and, as Mutually Agreed, the Seller shall exercise its rights under Section 10.1.1 of the License Agreement or, if applicable where Licensee was appointed the lead-party, Section 10.2.1 of the License Agreement, to assume the prosecution and maintenance of any such Applicable Patents, provided that Buyer shall pay all costs and expenses of such prosecution and maintenance (including costs and expenses of counsel).

(d) The Seller shall act as Mutually Agreed to (i) take any and all actions, and prepare, execute, deliver and file any and all agreements, documents and instruments, that are reasonably necessary or desirable to diligently prosecute, preserve and maintain any Licensed Patents in the European Territory for which it controls the prosecution and maintenance, including in accordance with Section 10.1.1 of the License Agreement and, if applicable Section 10.2.1 (where the Seller was appointed the lead-party or the Seller assumed such role from Licensee as permitted pursuant to Section 6.12(c) above) of the License Agreement, including payment of maintenance fees or annuities on any such Licensed Patents, which, as between the parties, shall be at the sole expense of the Buyer, (ii) prosecute any corrections, substitutions, reissues, reviews and reexaminations of any Licensed Patents in the European Territory, for which it controls the prosecution and maintenance, including in accordance with Section 10.1.1 of the License Agreement and, if applicable Section 10.2.1 (where the Seller was appointed the lead-party or the Seller assumed such role from Licensee as permitted pursuant to Section 6.12(c) above) of the License Agreement, and any other forms of patent term restoration in any applicable jurisdiction in the European Territory, (iii) diligently enforce and defend any Licensed Patents for which it controls the defense and enforcement in the European Territory, including by bringing any legal action for infringement or defending any counterclaim of invalidity or unenforceability or action of a third party for declaratory judgment of non-infringement or non-interference),and (iii) not disclaim or abandon, or fail to take any action necessary or desirable to prevent the disclaimer or abandonment (including through lack of enforcement against third party infringers), of any Licensed Patents in the European Territory for which it controls the prosecution and maintenance, including in accordance with Section 10.1.1 of the License Agreement and, if applicable Section 10.2.1 (where the Seller was appointed the lead-party or the Seller assumed such role from Licensee as permitted pursuant to Section 6.12(c) above) of

the License Agreement. For purposes of compliance with this Section 6.12(d), the Seller shall employ such counsel, reasonable acceptable to the Seller, as the Buyer shall recommend for such purpose, provided that Buyer shall pay all costs and expenses of any actions taken under this this Section 6.12(d) (including costs and expenses of counsel).

Efforts to Consummate Transactions

. Subject to the terms and conditions of this Agreement, each of the Seller and the Buyer shall use its commercially reasonable efforts to take, or cause to be taken, all actions and to do, or cause to be done, all things reasonably necessary under applicable law to consummate the transactions contemplated by this Agreement. Each of the Buyer and the Seller agrees to execute and deliver such other documents, certificates, agreements and other writings and to take such other actions as may be reasonably necessary in order to consummate or implement expeditiously the transactions contemplated by this Agreement.

Further Assurances

. After the Closing, the Seller and the Buyer agree to execute and deliver such other documents, certificates, agreements and other writings and to take such other actions as may be reasonably necessary in order to give effect to the transactions contemplated by this Agreement.

Tax Matters

.

(a) Notwithstanding anything to the contrary in the Transaction Documents, Seller and Purchaser shall treat the transactions contemplated by the Transaction Documents as a sale of the Royalty for United States federal, state, local and non-U.S. Tax purposes. Accordingly, any and all Royalty payments made pursuant to the License Agreement after the Closing Date shall be treated as made to Buyer for United States federal, state, local and non-U.S. Tax purposes. The Parties shall cooperate to effect the foregoing treatment for United States federal, state, local and non-U.S. Tax purposes in the event that, notwithstanding the Licensee Consent or Licensee Instruction, a Licensee, any Sublicensee or any other Person makes any future remittance of Royalty payments to Seller which Seller must remit to Buyer pursuant to Section 6.2(a) of this Agreement.

(b) To the extent any amount of the Royalty is withheld at source from a payment made pursuant to the License Agreement, as applicable, such withheld amount shall for all purposes of this Agreement be treated as paid to Buyer. Any amounts withheld pursuant to this Section 6.15(b) attributable to Buyer shall be credited for the account of Buyer. If there is an inquiry by any Governmental Entity of Buyer related to this Section 6.15(b), Seller shall cooperate with Buyer in responding to such inquiry in a reasonable manner consistent with this Section 6.15. Seller shall have no obligation to gross-up or otherwise pay Buyer any amounts with respect to source withholding. All amounts withheld as described herein shall for all purposes of this Agreement be deemed to have been received by Buyer.

(c) The Parties hereto agree not to take any position that is inconsistent with the provisions of this Section 6.15 on any Tax return or in any audit or other administrative or judicial proceeding unless (i) the other party hereto has consented to such actions or (ii) the party hereto that contemplates taking such an inconsistent position has been advised by nationally recognized tax counsel in writing that there is no “reasonable basis” (within the meaning of

Treasury Regulation Section 1.6662-3(b)(3)) for the position specified in this Section 6.15. If there is an inquiry by any Governmental Entity of Seller or Purchaser related to this Section 6.15, the parties hereto shall cooperate with each other in responding to such inquiry in a reasonable manner consistent with this Section 6.15.

ARTICLE 7
CONFIDENTIALITY

Confidentiality

. Except as provided in this ARTICLE 7 or otherwise agreed in writing by the parties, the parties hereto agree that each party (the "Receiving Party") shall keep confidential and shall not publish or otherwise disclose and shall not use for any purpose other than as provided for in this Agreement (which includes the exercise of any rights or the performance of any obligations hereunder) any information furnished to it by or on behalf of the other party (the "Disclosing Party") pursuant to this Agreement (such information, "Confidential Information" of the Disclosing Party), except for that portion of such information that:

(a) was already known to the Receiving Party, other than under an obligation of confidentiality, at the time of disclosure by the Disclosing Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the Receiving Party in breach of this Agreement;

(d) is independently developed by the Receiving Party or any of its Affiliates, as evidenced by written records, without the use of or reference of the Confidential Information; or

(e) is subsequently disclosed to the Receiving Party on a non-confidential basis by a Third Party without obligations of confidentiality with respect thereto.

Authorized Disclosure

.

(a) Either party may disclose Confidential Information with the prior written consent of the Disclosing Party or to the extent such disclosure is reasonably necessary in the following situations:

(i) prosecuting or defending litigation;

(ii) complying with applicable laws and regulations, including regulations promulgated by securities exchanges;

(iii) complying with a valid order of a court of competent jurisdiction or other Governmental Entity;

(iv) for regulatory, tax or customs purposes;

(v) for audit purposes, provided that each recipient of Confidential Information must be bound by customary obligations of confidentiality and non-use prior to any such disclosure;

(vi) disclosure to its Affiliates and Representatives on a need-to-know basis, provided that each recipient of Confidential Information must be bound by customary obligations of confidentiality and non-use prior to any such disclosure; or

(vii) regarding the terms and conditions of the License Agreement or this Agreement, to the Receiving Party's legal and financial advisors, and to any actual or prospective acquirers, investors, collaborators and lenders (as well as and to their respective legal and financial advisors who are obligated to keep such information confidential provided that the Receiving Party will be responsible for any disclosure of Confidential Information by any such Person inconsistent with the confidentiality obligations owed by the Receiving Party hereunder.

(b) Notwithstanding the foregoing, in the event the Receiving Party is required to make a disclosure of the Disclosing Party's Confidential Information pursuant to Sections 7.2(a)(i), (ii), (iii) or (iv), it will, except where impracticable, give reasonable advance notice to the Disclosing Party of such disclosure and use reasonable efforts to secure confidential treatment of such information. In any event, the Buyer shall not file any patent application based upon or using the Confidential Information of Seller provided hereunder.

ARTICLE 8
INDEMNIFICATION

General Indemnity

. Subject to Section 8.3, from and after the Closing:

(a) the Seller hereby agrees to indemnify, defend and hold harmless the Buyer and its Affiliates and its and their directors, managers, trustees, officers, agents and employees (the "Buyer Indemnified Parties") from, against and in respect of all Losses suffered or incurred by the Buyer Indemnified Parties to the extent arising out of or resulting from (i) any breach of any of the representations or warranties (in each case, when made) of the Seller in this Agreement and the Seller Closing Certificate and (ii) any breach of any of the covenants or agreements of the Seller in this Agreement; provided, however, that the foregoing shall exclude any indemnification to any Buyer Indemnified Party (i) that results from the gross negligence, willful misconduct, or fraud of any Buyer Indemnified Party or (ii) to the extent resulting from acts or omissions of Seller or any of its Affiliates based upon written instructions from any Buyer Indemnified Party (unless Seller is otherwise liable for such Losses pursuant to the terms of this Agreement); and

(b) the Buyer hereby agrees to indemnify, defend and hold harmless the Seller and its Affiliates and its and their directors, officers, agents and employees ("Seller Indemnified Parties") from, against and in respect of all Losses suffered or incurred by the Seller Indemnified Parties to the extent arising out of or resulting from (i) any breach of any of the representations or warranties (in each case, when made) of the Buyer in this Agreement and the Buyer Closing Certificate or (ii) any breach of any of the covenants or agreements of the Buyer in this Agreement; provided, however, that the foregoing shall exclude any indemnification to any Seller Indemnified Party (i) that results from the gross negligence, willful misconduct, or fraud of any Seller Indemnified Party or (ii) to the extent resulting from acts or omissions of Buyer or any of its Affiliates based upon written instructions from any Seller Indemnified Party (unless Buyer is otherwise liable for such Losses pursuant to the terms of this Agreement).

Notice of Claims

. If either a Buyer Indemnified Party, on the one hand, or a Seller Indemnified Party, on the other hand (such Buyer Indemnified Party on the one hand and such Seller Indemnified Party on the other hand being hereinafter referred to as an "Indemnified Party"), has suffered or incurred any Losses for which indemnification may be sought under this Article 8, the Indemnified Party shall so notify the other party from whom indemnification is sought under this Article 8 (the "Indemnifying Party") promptly in writing describing such Loss, the amount or estimated amount thereof, if known or reasonably capable of estimation, and the method of computation of such Loss, all with reasonable particularity and containing a reference to the provisions of this Agreement in respect of which such Loss shall have occurred. If any claim, action, suit or proceeding is asserted or instituted by or against a third party with respect to which an Indemnified Party intends to claim any Loss under this Article 8, such Indemnified Party shall promptly notify the Indemnifying Party of such claim, action, suit or proceeding and tender to the Indemnifying Party the defense of such claim, action, suit or proceeding. A failure by an Indemnified Party to give notice and to tender the defense of such claim, action, suit or proceeding in a timely manner pursuant to this Section 8.2 shall not limit the obligation of the Indemnifying Party under this Article 8, except to the extent such Indemnifying Party is actually prejudiced thereby.

Limitations on Liability

. No party hereto shall be liable for any consequential (including lost profits), punitive, special, indirect or incidental damages under this Article 8 (and no claim for indemnification hereunder shall be asserted) as a result of any breach or violation of any covenant or agreement of such party (including under this Article 8) in or pursuant to this Agreement. Notwithstanding the foregoing, the Buyer shall be entitled to make indemnification claims, in accordance with the procedures set forth in this Article 8, for Losses that include any portion of the Royalty that the Buyer was entitled to receive but did not receive timely or at all due to any indemnifiable events under this Agreement, and such portion of the Royalty shall not be deemed consequential, punitive, special, indirect, incidental damages or lost profits for any purpose of this Agreement. Other than with respect to any fraud, willful misconduct, or intentional misrepresentation, (a) in no event shall an Indemnifying Party's aggregate liability for Losses under Section 8.1(a) or Section 8.1(b) exceed the Purchase Price less the Royalty payments actually received by Buyer following the fourth anniversary of the date hereof, and (b) no Indemnifying Party shall have any liability for Losses under Section 8.1(a) or Section 8.1(b) unless and until the aggregate amount of all Losses incurred by the Indemnified Party equals or exceeds $[***], in which event such Indemnifying Party shall be liable for all Losses including such amount.

Third Party Claims

. Upon providing notice to an Indemnifying Party by an Indemnified Party pursuant to Section 8.2 of the commencement of any action, suit or proceeding against such Indemnified Party by a third party with respect to which such Indemnified Party intends to claim any Loss under this Article 8, such Indemnifying Party shall have the right to defend such claim, at such Indemnifying Party's expense and with counsel of its choice reasonably satisfactory to the Indemnified Party. If the Indemnifying Party assumes the defense of such claim, the Indemnified Party shall, at the request of the Indemnifying Party, use commercially reasonable efforts to cooperate in such defense; provided, that the Indemnifying Party shall bear the Indemnified Party's reasonable out-of-pocket costs and expenses incurred in connection with such cooperation. So long as the Indemnifying Party is conducting the defense of such claim as provided in this Section 8.4, the Indemnified Party may retain separate co-counsel at its expense and may participate in the defense of such claim, and neither the Indemnified Party nor the Indemnifying Party shall consent to the entry of any Judgment or enter into any settlement with respect to such claim without the prior written consent of the other unless such Judgment or settlement (A) provides for the payment by the Indemnifying Party of money as sole relief (if any) for the claimant (other than customary and reasonable confidentiality obligations relating to such claim, Judgment or settlement), (B) results in the full and general release of the Indemnified Party from all liabilities arising out of, relating to or in connection with such claim and (C) does not involve a finding or admission of any violation of any law, rule, regulation or Judgment, or the rights of any Person, and has no effect on any other claims that may be made against the Indemnified Party. In the event the Indemnifying Party does not or ceases to conduct the defense of such claim as so provided, (i) the Indemnified Party may defend against, and consent to the entry of any reasonable Judgment or enter into any reasonable settlement with respect to, such claim in any manner it may reasonably deem to be appropriate, (ii) subject to the limitations set forth in Section 8.3, the Indemnifying Party shall reimburse the Indemnified Party promptly and periodically for the reasonable out-of-pocket costs of defending against such claim, including reasonable attorneys' fees and expenses against reasonably detailed invoices, and (iii) the Indemnifying Party shall remain responsible for any Losses the Indemnified Party may suffer as a result of such claim to the full extent provided in this Article 8.

Exclusive Remedy

. Except as set forth in Section 10.10, from and after Closing, the rights of the parties hereto pursuant to (and subject to the conditions of) this Article 8 shall be the sole and exclusive remedy of the parties hereto and their respective Affiliates with respect to any claims (whether based in contract, tort or otherwise) resulting from or relating to any breach of the representations, warranties covenants and agreements made under this Agreement or any certificate, document or instrument delivered hereunder, and each party hereto hereby waives, to the fullest extent permitted under applicable law, and agrees not to assert after Closing, any other claim or action in respect of any such breach. Notwithstanding the foregoing, claims for fraud shall not be waived or limited in any way by this Article 8.

ARTICLE 9
TERMINATION

Grounds for Termination

. This Agreement may be terminated at any time prior to the Closing:

(a) by mutual written agreement of the Buyer and the Seller; or

(b) by the Buyer upon notice in writing to the Seller at any time after December 31, 2019, if by such date the Closing shall not have been consummated for any reason other than a material breach by the Buyer of any of its representations, warranties, covenants, agreements or obligations under this Agreement.

Automatic Termination

. Unless earlier terminated as provided in Section 9.1, this Agreement shall continue in full force and effect until the Royalty Termination Date, at which point this Agreement shall automatically terminate, except with respect to any rights that shall have accrued prior to such termination.

Survival

. Notwithstanding anything to the contrary in this Article 9, the following provisions shall survive termination of this Agreement: Section 6.1 (Disclosures), Section 6.2(b) (Payments Received in Error; Interest), Article 7 (Confidentiality), Article 8 (Indemnification), Section 9.3 (Survival) and Article 10 (Miscellaneous). Termination of the Agreement shall not relieve any party of liability in respect of breaches under this Agreement by any party on or prior to termination.

ARTICLE 10
MISCELLANEOUS

Notices

. All notices and other communications under this Agreement shall be in writing and shall be by email with PDF attachment, facsimile, courier service or personal delivery to the following addresses, or to such other addresses as shall be designated from time to time by a party hereto in accordance with this Section 10.1:

If to the Seller, to it at:

Ultragenyx Pharmaceutical
60 Leveroni Court
Novato, CA 94949
Attention: Karah Parschauer
Email: kparschauer@ultragenyx.com

With a copy to:

Gibson, Dunn & Crutcher LLP
555 Mission Street
San Francisco, CA 94105
Attention: Ryan Murr
Email: rmurr@gibsondunn.com

If to the Buyer, to it at:

RP Management, LLC
110 E. 59th Street, Suite 3300
New York, New York 0022

Attention: George Lloyd
Email: glloyd@royaltypharma.com

With a copy to:
Goodwin Procter LLP
100 Northern Avenue
Boston, Massachusetts 02210
Attention: Arthur R. McGivern & Karen A. Spindler
Email: amcgivern@goodwinlaw.com; kspindler@goodwinlaw.com

All notices and communications under this Agreement shall be deemed to have been duly given (i) when delivered by hand, if personally delivered, (ii) when received by a recipient, if sent by email, (iii) when sent, if sent by facsimile, with an acknowledgement of sending being produced by the sending facsimile machine or (iv) one Business Day following sending within the United States by overnight delivery via commercial one-day overnight courier service.

Expenses

. Except as otherwise provided herein, all fees, costs and expenses (including any legal, accounting and banking fees) incurred in connection with the preparation, negotiation, execution and delivery of this Agreement and to consummate the transactions contemplated hereby shall be paid by the party hereto incurring such fees, costs and expenses.

Assignment

. The Seller shall not sell, assign or otherwise transfer (a) all or any portion of its interest in the Joint Invention Patents, (b) all or any portion of its interest in the License Agreement that relates to the Royalty or to the European Territory, (c) all or any portion of its interest in this Agreement or (d) all or any portion of its interest in the License Agreement that does not relate to the Royalty or to the European Territory (but only, in the case of clause (d), if the sale, assignment or transfer of such portion would reasonably be expected (with or without the giving of notice or the passage of time, or both) to have a Material Adverse Effect) to any third party or to the Licensee by operation of law, merger, change of control, or otherwise, unless in connection therewith (a) such Person acquires all of the Seller's interest in all of the Joint Invention Patents, the License Agreement and this Agreement and (b) prior to closing any such transaction, the Seller causes such Person to deliver a writing to the Buyer in which (i) if such Person is not the Licensee, such Person assumes all of the obligations of the Seller to the Buyer under this Agreement, and (ii) if such Person is the Licensee, the Licensee assumes all of the obligations of the Seller to the Buyer hereunder and agrees to pay the Royalty directly to the Buyer notwithstanding any subsequent termination of the License Agreement by the Licensee. Subject to the first sentence of this Section 10.3, this Agreement shall be binding upon, inure to the benefit of and be enforceable by, the parties hereto and their respective permitted successors and assigns. The Buyer may assign this Agreement, provided that the Buyer promptly thereafter notifies the Seller and any such assignee promptly thereafter agrees in writing to be bound by the obligations of the Buyer contained in this Agreement, and in any event such assignment shall be of the Agreement in its entirety. Any purported assignment in violation of this Section 10.3 shall be null and void.

Amendment and Waiver

.

(a) This Agreement may be amended, modified or supplemented only in a writing signed by each of the parties hereto. Any provision of this Agreement may be waived only in a writing signed by the parties hereto granting such waiver.

(b) No failure or delay on the part of any party hereto in exercising any right, power or remedy hereunder shall operate as a waiver thereof, nor shall any single or partial exercise of any such right, power or remedy preclude any other or further exercise thereof or the exercise of any other right, power or remedy. No course of dealing between the parties hereto shall be effective to amend, modify, supplement or waive any provision of this Agreement.

Entire Agreement

. This Agreement, the Exhibits annexed hereto and the Disclosure Schedule constitute the entire understanding between the parties hereto with respect to the subject matter hereof and supersede all other understandings and negotiations with respect thereto.

No Third Party Beneficiaries

. This Agreement is for the sole benefit of the Seller and the Buyer and their permitted successors and assigns and nothing herein expressed or implied shall give or be construed to give to any Person, other than the parties hereto and such successors and assigns, any legal or equitable rights hereunder.

Governing Law

. This Agreement shall be governed by, and construed in accordance with, the laws of the State of New York without giving effect to any choice or conflict of law provision or rule that would cause the application of the laws of any other jurisdiction.

JURISDICTION; VENUE

.

(a) EACH OF THE PARTIES HERETO HEREBY IRREVOCABLY AND UNCONDITIONALLY SUBMITS, FOR ITSELF AND ITS RESPECTIVE PROPERTY AND ASSETS, TO THE EXCLUSIVE JURISDICTION OF ANY NEW YORK STATE COURT OR FEDERAL COURT OF THE UNITED STATES OF AMERICA SITTING IN NEW YORK COUNTY, NEW YORK, AND ANY APPELLATE COURT THEREOF, IN ANY ACTION OR PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT, OR FOR RECOGNITION OR ENFORCEMENT OF ANY JUDGMENT IN RESPECT THEREOF, AND THE BUYER AND THE SELLER HEREBY IRREVOCABLY AND UNCONDITIONALLY AGREE THAT ALL CLAIMS IN RESPECT OF ANY SUCH ACTION OR PROCEEDING MAY BE HEARD AND DETERMINED IN ANY SUCH NEW YORK STATE COURT OR, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, IN SUCH FEDERAL COURT. THE BUYER AND THE SELLER HEREBY AGREE THAT A FINAL JUDGMENT IN ANY SUCH ACTION OR PROCEEDING SHALL BE CONCLUSIVE AND MAY BE ENFORCED IN OTHER JURISDICTIONS BY SUIT ON THE JUDGMENT OR IN ANY OTHER MANNER PROVIDED BY APPLICABLE LAW. EACH OF THE BUYER AND THE SELLER HEREBY SUBMITS TO THE EXCLUSIVE PERSONAL JURISDICTION AND VENUE OF SUCH NEW YORK STATE AND FEDERAL COURTS. THE BUYER AND THE SELLER AGREE, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, THAT PROCESS MAY BE SERVED ON THE BUYER OR THE SELLER IN THE

SAME MANNER THAT NOTICES MAY BE GIVEN PURSUANT TO SECTION 10.1 HEREOF.

(b) EACH OF THE PARTIES HERETO HEREBY IRREVOCABLY AND UNCONDITIONALLY WAIVES, TO THE FULLEST EXTENT IT MAY LEGALLY AND EFFECTIVELY DO SO, ANY OBJECTION THAT IT MAY NOW OR HEREAFTER HAVE TO THE LAYING OF VENUE OF ANY ACTION OR PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT IN ANY NEW YORK STATE OR FEDERAL COURT. EACH OF THE BUYER AND THE SELLER HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, THE DEFENSE OF AN INCONVENIENT FORUM TO THE MAINTENANCE OF SUCH ACTION OR PROCEEDING IN ANY SUCH COURT.

Severability

. If any term or provision of this Agreement shall for any reason be held to be invalid, illegal or unenforceable in any situation in any jurisdiction, then, to the extent that the economic and legal substance of the transactions contemplated hereby is not affected in a manner that is materially adverse to either party hereto, all other terms and provisions of this Agreement shall nevertheless remain in full force and effect and the enforceability and validity of the offending term or provision shall not be affected in any other situation or jurisdiction.

Specific Performance

. Each of the parties acknowledges and agrees that the other parties would be damaged irreparably in the event any of the provisions of this Agreement are not performed in accordance with their specific terms or otherwise are breached or violated. Accordingly, notwithstanding Section 8.5, each of the parties agrees that, without posting bond or other undertaking, the other parties shall be entitled to an injunction or injunctions to prevent breaches or violations of the provisions of this Agreement and to enforce specifically this Agreement and the terms and provisions hereof in any action, suit or other proceeding instituted in any court of the United States or any state thereof having jurisdiction over the parties and the matter in addition to any other remedy to which it may be entitled, at law or in equity. Each party further agrees that, in the event of any action for specific performance in respect of such breach or violation, it shall not assert that the defense that a remedy at law would be adequate.

Trustee Capacity of Wilmington Trust Company

. Notwithstanding anything contained herein to the contrary, it is expressly understood and agreed by the parties hereto that (i) this Agreement is executed and delivered by Wilmington Trust Company, not individually or personally but solely in its trustee capacity, in the exercise of the powers and authority conferred and vested in it under the trust deed of the Buyer, (ii) each of the representations, undertakings and agreements herein made on the part of the Buyer is made and intended not as a personal representation, undertaking and agreement by Wilmington Trust Company but is made and intended for the purpose of binding only the Buyer and (iii) under no circumstances shall Wilmington Trust Company be personally liable for the payment of any indebtedness or expenses of the Buyer or be liable for the breach or failure of any obligation, representation, warranty or covenant made or undertaken by the Buyer under this Agreement or any related documents.

Counterparts. This Agreement may be executed in any number of counterparts and by the parties hereto in separate counterparts, each of which when so executed shall be deemed to be an original and all of which taken together shall constitute one and the same agreement. Copies of executed counterparts transmitted by telecopy, facsimile or other similar means of electronic transmission, including "PDF," shall be considered original executed counterparts, provided receipt of such counterparts is confirmed.

[Signature Page Follows]

IN WITNESS WHEREOF, the parties hereto have caused this Royalty Purchase Agreement to be executed and delivered by their respective representatives thereunto duly authorized as of the date first above written.

ULTRAGENYX PHARMACEUTICAL INC.

By: /s/ Shalini Sharp
Name: Shalini Sharp
Title: Chief Financial Officer and Executive Vice President

RPI FINANCE TRUST

By: Wilmington Trust Company, not in its individual capacity but solely in its capacity as owner trustee

By: /s/ Erwin M. Soriano
Name: Erwin M. Soriano
Title: Vice President

Exhibit 10.70

WOBURN MCB II, LLC

Lease To

ULTRAGENYX PHARMACEUTICAL INC.

THE SUBMISSION OF THIS LEASE FOR EXAMINATION, REVIEW, NEGOTIATION AND/OR SIGNATURE SHALL NOT CONSTITUTE AN OFFER OR AN OPTION TO LEASE OR A RESERVATION OF THE PREMISES AND IS SUBJECT TO WITHDRAWAL OR MODIFICATION AT ANY TIME BY EITHER PARTY. THIS LEASE SHALL BECOME EFFECTIVE AND BINDING ONLY IF AND WHEN IT SHALL BE EXECUTED AND DELIVERED BY BOTH LANDLORD AND TENANT.

150 Presidential Way,
Woburn, Massachusetts
Office Lease

Table of Contents by Articles and Sections

150 Presidential Way,
Woburn, Massachusetts
LEASE EXHIBITS

150 Presidential Way,
Woburn, Massachusetts

OFFICE LEASE
STANDARD FORM

THIS LEASE by and between Woburn MCB II, LLC a Massachusetts limited liability company ("Landlord") having a principal place of business at C/O Eastport Real Estate Services, Inc., 107 Audubon Road, Wakefield, MA 01880, and Ultragenyx Pharmaceutical, Inc. ("Tenant").

W I T N E S S E T H:

ARTICLE 1
Reference Data and Definitions

1.01 Reference Data

LANDLORD:	Woburn MCB II, LLC
LANDLORD'S ADDRESS: (FOR PAYMENT OF RENT)	Woburn MCB II, LLC C/O Eastport Real Estate Services, Inc. 107 Audubon Road, Suite 2-301 Wakefield, Massachusetts 01880
LANDLORD'S ADDRESS (FOR NOTICE):	Mr. Robert M. Bowen Eastport Real Estate Services, Inc. 107 Audubon Road Wakefield, MA 01880 With a copy to: Michael J. Novaria, Esq. Rubin and Rudman LLP 53 State Street, 15th Floor Boston, MA 02109
TENANT:	Ultragenyx Pharmaceutical, Inc.
TENANT'S ADDRESS (FOR NOTICE):	60 Leveroni Court Novato, CA 94949 With a copy to: Goodwin Procter LLP Attn: Chad Vella, Esq. 100 Northern Avenue Boston, Massachusetts 02210
PREMISES:	The portion of the Building located at 150 Presidential Way, Woburn MA consisting of the entire 4th floor of the Building plus the square footage

area of the duct chases on the 5th floor, as shown on Exhibit B attached hereto.

RENTABLE AREA OF PREMISES: Approximately 30,544 Rentable Square Feet on the 4th Floor and 98 Rentable Square Feet on the 5th Floor, totaling 30,642 Rentable Square Feet.

TERM COMMENCEMENT DATE: July 1, 2019

RENT COMMENCEMENT DATE: October 1, 2019

STATED EXPIRATION DATE: The date that is eighty-eight (88) full calendar months after the Term Commencement Date

RENTABLE AREA OF THE BUILDING: Approximately 146,757 Square Feet.

BASIC RENT (subject to Section 4.03): SEE SCHEDULE BELOW

MONTHS	MONTHLY RENT	ANNUAL RENT
July 1, 2019 – September 30, 2019	**$0.00**	**$0.00**
October 1, 2019 – September 30, 2020	**$79,158.50**	**$949,902.00**
October 1, 2020 – September 30, 2021	**$81,712.00**	**$980,544.00**
October 1, 2021 – September 30, 2022	**$84,265.50**	**$1,011,186.00**
October 1, 2022 – September 30, 2023	**$86,819.00**	**$1,041,828.00**
October 1, 2023 – September 30, 2024	**$89,372.50**	**$1,072,470.00**
October 1, 2024 – September 30, 2025	**$91,926.00**	**$1,103,112.00**
October 1, 2025 - September 30, 2026	**$94,479.50**	**$1,133,754.00**
October 1, 2026 – December 31, 2026	**$97,033.00**	**$1,164,396.00**

ESTIMATED COST OF ELECTRICAL SERVICE: Beginning on the Term Commencement Date, Premises will be separately metered for electricity via check metering or direct meter from the utility providing service.

INITIAL MONTHLY PAYMENT (Basic Rent):	$79,158.50
TAX BASE:	The Taxes for the fiscal year 2020.
OPERATING EXPENSE BASE:	The Operating Expenses for Calendar Year 2019.
TENANT'S SHARE:	20.88%
SECURITY DEPOSIT:	Letter of Credit in the amount of $395,262.90
PERMITTED USES:	General office uses consistent with a comparable office building located in the Woburn market and research and development uses, including a biotechnical and Uniform Building Code ("UBC") "B" laboratory use classified as BSL-2 and uses ancillary thereto. Tenant's Permitted Uses shall include the Tenant's right to receive shipments of BSL-2 materials and the transmission of such materials into the Premises at any time, which materials shall be packaged and labelled in an industry-standard method.

1.02 General Provisions.

For all purposes of the Lease unless otherwise expressed and provided herein or therein or unless the context otherwise requires:

(a) The words herein, hereof, hereunder and other words of similar import refer to the Lease as a whole and not to any particular article, section or other subdivision of this Lease.

(b) A pronoun in one gender includes and applies to the other genders as well.

(c) Each definition stated in Section 1.01 or 1.03 of this Lease applies equally to the singular and the plural forms of the term or expression defined.

(d) Any reference to a document defined in Section 1.03 of this Lease is to such document as originally executed, or, if modified, amended or supplemented in accordance with the provisions of this Lease, to such document as so modified, amended or supplemented and in effect at the relevant time of reference thereto.

(e) All accounting terms not otherwise defined herein have the meanings assigned to them in accordance with generally accepted accounting principles.

(f) All references in Section 1.01 hereof are subject to the specified definitions thereof (if any) in Section 1.03 hereof.

1.03 Terms Defined.

Each term or expression set forth above in Section 1.01 hereof or below in this Section 1.03 has the meaning stated immediately after it.

Additional Rent. All sums which Tenant shall be obligated to pay hereunder other than Basic Rent.

Additional Services. Services provided to Tenant or in respect to the Premises which are in addition to the services described in Exhibit D hereto.

Adjusted Operating Expense Base. The amount determined by multiplying the Operating Expense Base by the Adjustment Factor.

Adjusted Tax Base. The amount determined by multiplying the Tax Base by the Adjustment Factor.

Adjustment Factor. With respect to the First Calendar Year and the Last Calendar Year, the percentage computed by dividing the number of days of each such period falling within the Lease term by 365. For all other calendar years, the Adjustment Factor shall be 100%.

Affiliate. With respect to any specified Person, any other Person directly or indirectly controlling or controlled by or under direct or indirect common control with such specified Person. For the purposes of this definition, the term "control", when used with respect to any specified Person, means the power to direct the management and policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract or otherwise, and the terms "controlling" and "controlled by" have meanings correlative to the foregoing.

Authorizations. All franchises, licenses, permits and other governmental consents issued by Governmental Authorities pursuant to Legal Requirements which are or may be required for the use and occupancy of the Premises or the conduct or continuation of a Permitted Use therein.

Basic Services. The services described in Exhibit D hereto.

Building. The building located at 150 Presidential Way, Woburn, Massachusetts.

Business Day. A day which is not a Saturday, Sunday or other day on which banks in Boston, Massachusetts, are authorized or required by law or executive order to remain closed.

Calendar Year. The First Calendar Year, the Last Calendar Year and each full calendar year (January 1 through December 31) occurring during the Lease Term.

C.P.I. "Consumer Price Index - All Urban Consumers - (CPI-U) - U.S. City Average - All Items (1982-1984=100)" as published by the U.S. Department of Labor.

Common Areas. All interior and exterior areas devoted to the common use of occupants of the Building or the provision of Services to the Building, including but not limited to all corridors, elevator foyers, air shafts, elevator shafts, and elevators, stairwells and stairs, mechanical rooms, janitor closets, vending areas, driveways, parking areas and other similar facilities for the provision of Services or for the use of all occupants of multi-tenant floors or all occupants of the Building.

Control. As defined in the definition of Affiliate.

Corporation. A corporation, company, association, limited liability company, business trust or similar organization wherever formed.

Default. Any event or condition specified in Article 20 hereof so long as any applicable requirement for the giving of notice or lapse of time or both have not been fulfilled.

Event of Default. Any event or condition specified in (a) Article 20 hereof (if all applicable periods for the giving of notice or lapse of time or both have expired) or (b) in Article 21 hereof.

First Calendar Year. The partial Calendar Year period commencing on the Term Commencement Date and ending on the next succeeding December 31.

Force Majeure. Acts of God, strikes, lockouts, labor troubles, inability to procure materials, failure of power, government-ordered restrictions on utility usage, riots and insurrection, acts of public enemy, wars, earthquakes, hurricanes and other natural disasters, fires, explosions, other causes beyond a party's reasonable control (which shall not include existing physical conditions at the Building), or any act, failure to act or Default of the other party to this Lease; provided, however, lack of money shall not be deemed such a cause.

General Contractor. A general contractor to be selected by Tenant and approved by Landlord, which approval shall not be unreasonably withheld, conditioned or delayed.

Governmental Authority. United States of America, the Commonwealth of Massachusetts, the City of Woburn, County of Middlesex, and any political subdivision thereof and any agency, department, commission, board, bureau or instrumentality of any of them.

Insolvency. The occurrence with respect to any Person of one or more of the following events: the death, dissolution, termination of existence (other than by merger or consolidation), insolvency, appointment of a receiver for all or substantially all of the property of such Person, the making of a fraudulent conveyance or the execution of an assignment or trust mortgage for the benefit of creditors by such Person, or the filing of a petition in bankruptcy or the commencement of any proceedings by or against such Person under a bankruptcy, insolvency or other law relating to the relief or the adjustment of indebtedness, rehabilitation or reorganization of debtors; provided that if such petition or commencement is involuntarily made against such a Person and is dismissed within sixty (60) days of the date of such filing or commencement, such events shall not constitute an Insolvency hereunder.

Insurance Requirements. All terms of any policy of insurance maintained by Landlord or Tenant and applicable to (or affecting any condition, operation, use or occupancy of) the Building or the Premises or any part or parts of either and all requirements of the issuer of any such policy and all orders, rules, regulations and other requirements of the National Board of Fire Underwriters (or any other body exercising similar functions).

Land. The land located at 150 Presidential Way, Woburn, Massachusetts, County of Middlesex, Commonwealth of Massachusetts, described in Exhibit A.

Landlord's Work. The work to be done by Landlord with respect to the Premises shown on Exhibit B, described in Section 7.01 and Exhibit C.

Last Calendar Year. The partial Calendar Year commencing on January 1 of the Calendar Year in which the Lease Termination Date occurs and ending on the Lease Termination Date.

Lease Term. The period commencing on the Term Commencement Date and ending on the Lease Termination Date.

Lease Termination Date. The earliest to occur of (1) the Stated Expiration Date, (2) the termination of this Lease by Landlord as the result of an Event of Default, or (3) the termination of this Lease pursuant to Article 17 (Damage or Destruction) or 18 (Eminent Domain) hereof.

Lease Year. A period commencing on the Term Commencement Date (or an anniversary thereof) and ending on the day before the next succeeding anniversary thereof. For example, the first Lease Year is a period commencing on the Term Commencement Date and ending on the day before the first anniversary thereof. The last Lease Year shall end on the Lease Termination Date.

Legal Requirements. All laws, statutes, codes, ordinances (and all rules and regulations thereunder), all executive orders and other administrative orders, judgments, decrees, injunctions and other judicial orders of or by any Governmental Authority which may at any time be applicable to the Land, the Building or the Premises or to any condition or use thereof and the provisions of all Authorizations.

Occupancy Arrangement. With respect to the Premises or any portion thereof, and whether (a) written or unwritten or (b) for all or any portion of the Lease Term, an assignment, a sublease, a tenancy at will, a tenancy at sufferance, or any other arrangement (including but not limited to a license or concession) pursuant to which a Person occupies, or shall have the right to occupy, the Premises for any purpose.

Operating Expenses. Beginning on the Term Commencement Date, all expenses, costs, and disbursements of every kind and nature which Landlord shall pay or become obligated to pay in connection with the ownership, operation and maintenance of the Land and the Building (including all parking facilities in operation on the Term Commencement Date and such additional parking facilities which are necessary or beneficial for the operation of the Land and Building) and the provision of Basic Services, including, but not limited to (a) wages, salaries, fees and costs to Landlord of all Persons engaged in connection therewith, including taxes, insurance, and benefits relating thereto; (b) the cost of (i) all supplies and materials, electricity and lighting, (ii) water, heat, air conditioning, and ventilating, (iii) all maintenance, janitorial, and service agreements, (iv) all insurance, including the cost of casualty and liability insurance, (v) repairs, replacements and maintenance, including, without limitation, Landlord's costs and expenses of performing its obligations under Section 8.01 (including, without limitation, costs and expenses which may be capital in nature), (vi) capital items which are primarily for the purpose of reducing Operating Expenses or which may be required by a Governmental Authority, amortized over the reasonable life of the capital items with the reasonable life and amortization schedule being determined by Landlord in accordance with generally accepted accounting principles (provided that in the event the reasonably estimated annual savings arising from the installation of any such capital improvement intended to reduce Operating Expenses shall exceed such annual amortization, Operating Expenses shall include, in lieu of such amortization, such estimated annual savings until the cost of such improvement shall have been completely amortized), (vii) pursuing an application for an abatement of taxes pursuant to Section 6.05 hereof to the extent not deducted from the abatement, if any, received; (c) management fees of 5% of gross revenues from the Building; and (d) the cost to Landlord of operating, repairing and maintaining exterior common areas and facilities which may not be located entirely on the Land but which may be used for parking or for landscaping, security and maintenance for common roadways and open areas. Operating Expenses shall not include specific costs billed to and paid by specific tenants. If at any time during the Term, less than ninety-five percent (95%) of the Rentable Area of the Building is occupied, Operating Expenses shall be adjusted by the Landlord to reasonably approximate the Operating Expenses which would be incurred if the Building had been at least ninety-five percent (95%) occupied. Notwithstanding anything to the contrary set forth in this Lease, Operating Expenses shall not include the following: (I) any ground or underlying lease rental; (II) bad debt expenses

and interest, principal, points and fees on debts or amortization on any mortgage or other debt instrument encumbering the Building or the Land; (III) costs which may be considered capital improvements, capital repairs, capital changes or any other capital costs as determined under generally accepted accounting principles except for capital improvements required by any laws not in existence and not in effect as of the Term Commencement Date, in which case such costs shall be capitalized and amortized over their useful life determined in accordance with generally accepted accounting principles; (IV) rentals for items which if purchased, rather than rented, would constitute a capital cost; (V) costs incurred by Landlord to the extent that Landlord is reimbursed by insurance proceeds or is otherwise reimbursed; (VI) depreciation, amortization and interest payments, except on equipment, materials, tools, supplies and vendor-type equipment purchased by Landlord to enable Landlord to supply services Landlord might otherwise contract for with a third party where such depreciation, amortization and interest payments would otherwise have been included in the charge for such third party's services, all as determined in accordance with generally accepted accounting principles, consistently applied, and when depreciation or amortization is permitted or required, the item shall be amortized over its reasonably anticipated useful life; (VII) advertising and promotional expenditures, and costs of acquisition and maintenance of signs in or on the Building identifying the owner of the Building or other tenants; (VIII) marketing costs, including leasing commissions, attorneys' fees (in connection with the negotiation and preparation of letters, deal memos, letters of intent, leases, subleases and/or assignments), space planning costs, and other costs and expenses incurred in connection with lease, sublease and/or assignment negotiations and transactions with present or prospective tenants or other occupants of the Building; (IX) costs, including permit, license and inspection costs, incurred with respect to the installation of other tenants' or other occupants' improvements or incurred in renovating or otherwise improving, decorating, painting or redecorating vacant space for tenants or other occupants of the Building; (X) expenses in connection with services or other benefits which are not offered to Tenant or for which Tenant is charged for directly; (XI) costs incurred by Landlord due to the violation by Landlord or any tenant of the terms and conditions of any lease of space in the Building; (XII) management fees paid or charged by Landlord in connection with the management of the Building to the extent such management fee is in excess of the management fee customarily paid or charged by landlords of comparable buildings in the vicinity of the Building; (XIII) salaries and other benefits paid to the employees of Landlord to the extent customarily included in or covered by a management fee, provided that in no event shall Operating Expenses include salaries and/or benefits attributable to personnel above the level of Property manager; (XIV) rent for any office space occupied by Building management personnel to the extent the size or rental rate for of such office space exceeds the size or fair market rental value of office space occupied by management personnel of comparable buildings in the vicinity of the Building; (XV) amounts paid to Landlord or to subsidiaries or affiliates of Landlord for goods and/or services in the Building to the extent the same exceeds the costs of such goods and/or services rendered by unaffiliated third parties on a competitive basis; (XVI) Landlord's general corporate overhead and general and administrative expenses; (XVII) any compensation paid to clerks, attendants or other persons in commercial concessions operated by Landlord; (XVIII) services provided, taxes, attributable to, and costs incurred in connection with the operation of any retail, restaurant and garage operations for the Building, and any replacement garages or parking facilities and any shuttle services; (XIX) costs incurred in connection with upgrading the Building to comply with laws, rules, regulations and codes in effect prior to the Term Commencement Date; (XX) all assessments and premiums which are not specifically charged to Tenant because of what

Tenant has done, which can be paid by Landlord in installments, shall be paid by Landlord in the maximum number of installments permitted by law and not included as Operating Expenses except in the year in which the assessment or premium installment is actually paid; (XXI) costs arising from the negligence or willful misconduct of Landlord or other tenants or occupants of the Building or their respective agents, employees, licensees, vendors, contractors or providers of materials or services; (XXII) costs arising from Landlord's charitable or political contributions; (XXIII) costs arising from latent defects or repair thereof; (XXIV) costs for sculpture, paintings or other objects of art; (XXV) costs associated with the operation of the business of the entity which constitutes Landlord as the same are distinguished from the costs of operation of the Building, including accounting and legal matters, costs of defending any lawsuits with any mortgagee (except as the actions of Tenant may be in issue), costs of selling, syndicating, financing, mortgaging or hypothecating any of Landlord's interest in the Building, costs incurred in connection with any disputes between Landlord and its employees, between Landlord and Building management, or between Landlord and other tenants or occupants; (XXVI) costs of independent auditors; (XXVIII) any other costs or expenses which would not normally be treated as Operating Expenses by landlords of comparable buildings in the vicinity of the Building.

Partial Taking. Any Taking which is not a Total Taking.

Permitted Exceptions. Any liens or encumbrances on the Premises in the nature of (a) liens for taxes assessed but not yet due and payable, (b) easements, reservations, restrictions and rights of way encumbering or affecting the Land on the date of this Lease, (c) the rights of Landlord, Tenant and any other Person to whom Landlord has granted such rights to exercise in common with respect to the Land and the Common Areas the rights granted to Tenant hereunder, (d) mortgages of record, and (e) Title Conditions, so long as the same do not adversely impact Tenant's use of the Land, Building and Premises for the conduct of its business.

Person. An individual, a Corporation, a company, a voluntary association, a partnership, a trust, an unincorporated organization or a government or any agency, instrumentality or political subdivision thereof.

Premises. The space in the Building shown on Exhibit B hereto.

Proceeds. With respect to any Taking or occurrence described in Article 17 hereof, with respect to which any Person is obligated to pay any amount to or for the account of Landlord, the aggregate of (i) all sums payable or receivable under or in respect of any insurance policy, and (ii) all sums or awards payable in respect to a Taking.

Rent. Basic Rent and all Additional Rent.

Rentable Area of the Premises. The number of square feet stated in Section 1.01, whether the same should be more or less as a result of minor variations resulting from actual construction and completion of the Building or Premises so long as such work is done in accordance with the terms and provisions hereof. The calculation was made according to the following formula:

(i)On single tenant floors, the usable area measured from the inside surfaces of the outer glass of the Building, plus Tenant's Share of interior Common Areas.

(ii)On multi-tenant floors, the usable area measured from the inside surface of the outer glass of the Building to the midpoint of all demising walls of the space being measured plus the area of each corridor adjacent to and required as the result of the

layout of the space being measured, measured from the midpoint of the adjacent demising walls, plus Tenant's Share of interior Common Areas.

Rules and Regulations. Reasonable rules and regulations promulgated by Landlord and uniformly applicable to persons occupying the Building regulating the details of the operation and use of the Building, which rules and regulations shall not impact Tenant's use of the Premises for the Permitted Uses. The initial Rules and Regulations are attached hereto as Exhibit E.

Services. Basic Services and Additional Services.

Stated Expiration Date. The Stated Expiration Date set forth in Section 1.01.

Taking. The taking or condemnation of title to all or any part of the Land or the possession or use of the Building or the Premises by a Person for any public use or purpose or any proceeding or negotiations which might result in such a taking or any sale or lease in lieu of or in anticipation of such a taking.

Taxes. Beginning on the Term Commencement Date, all taxes, special or general assessments, water rents, rates and charges, sewer rents and other impositions and charges imposed by Governmental Authorities of every kind and nature whatsoever, extraordinary as well as ordinary, and each and every installment thereof which shall or may during the term of this Lease be charged, levied, laid, assessed, imposed, become due and payable or become liens upon or for or with respect to the Land or any part thereof or the Building or the Premises, appurtenances or equipment owned by Landlord thereon or therein or any part thereof or on this Lease under or by virtue of all present or future Legal Requirements or a tax based on a percentage, fraction or capitalized value of the Rent (whether in lieu of or in addition to the taxes hereinbefore described). Taxes shall not include inheritance, estate, excise, succession, transfer, gift, franchise, income, gross receipt, or profit taxes except to the extent such are in lieu of or in substitution for Taxes as now imposed on the Building, the Land, the Premises or this Lease. If for any year, including the Tax Base Year, Taxes have been reduced or abated, or are subsequently reduced or abated, because of vacancies in the Building, Taxes for such year shall be adjusted by Landlord to reasonably approximate the amount Taxes would have been had such vacancies not existed. Any assessments which can be paid in installments by Landlord shall be paid by Landlord in the maximum number of installments permitted by law and not included in Taxes except in the year in which the assessment is actually paid.

Tenant. As defined in the preamble hereof.

Tenant's Share. Tenant's Share shall be equal to the Rentable Area of the Premises divided by the Rentable Area of the Building.

Term Commencement Date. The Term Commencement Date stated in Section 1.01.

Title Conditions. All covenants, agreements, restrictions, easements and declarations of record on the date hereof so far as the same may be from time to time in force and applicable and which shall not impact Tenant's use of the Premises for the Permitted Uses.

Total Taking. (i) a Taking of: (a) the fee interest in all or substantially all of the Land or Building or (b) such title to, easement in, over, under or such rights to occupy and use any part or parts of the Land or Building to the exclusion of Landlord as shall have the effect, in the good faith judgment of the Landlord, of rendering the portion of the Land or Building remaining after such Taking (even if restoration were made) unsuitable for the continued use and occupancy of the

Building for the Permitted Uses or (ii) a Taking of all or substantially all of the Premises or such title to or easement in, on or over the Premises to the exclusion of Tenant which in the good faith judgment of the Landlord prohibits access to the Premises or the exercise by Tenant of its rights under this Lease.

ARTICLE 2
Premises

2.01 Premises.

Landlord hereby leases and lets to Tenant, and Tenant hereby takes and hires from Landlord, upon and subject to the terms, conditions, covenants and provisions hereof, the Premises subject to the Permitted Exceptions. Landlord reserves the right to install within or without the Premises pipes, ducts, vents, flues, conduits, wires and appurtenant fixtures which service the Premises and/or other parts of the Building; provided that such work and installations are done in such a manner that they do not unreasonably interfere with Tenant's use of the Premises.

2.02 Appurtenances.

Tenant, in common with others entitled thereto from time to time, may use the Common Areas for the purposes for which they were designed.

Landlord reserves the right, from time to time, to grant easements affecting the Land, to change or alter the boundaries of the Land and to alter, and grant to others the right to use, the entrances, parking areas and driveways on the Land, all for purposes of developing and using properties adjacent to the Land, so long as the same do not unreasonably interfere with Tenant’s use of the Common Areas or Premises or reduce the number of parking spaces available for Tenant.

2.03 Reservations By Landlord.

Landlord reserves the right, exercisable at any time and from time to time without the same constituting an actual or constructive eviction and without incurring any liability therefor or otherwise affecting Tenant’s obligations under this Lease, to make changes, alterations, additions, improvements, repairs or replacements to the Building and the Common Areas as long as such work does not unreasonably interfere with Tenant’s business, including, without limitation, elimination of Common Areas and changing the size, arrangement and location of, and eliminating, entrances, lobbies, driveways, parking areas, doors, corridors, elevators, stairs and restrooms.

ARTICLE 3
Term

3.01 Term Commencement.

The Lease Term shall commence on the Term Commencement Date as stated in Section 1.01.

3.02 Termination.

The Lease Term shall end on the Lease Termination Date.

3.03 Early Access.

Tenant shall have access to the Premises upon execution of this Lease by Tenant and Landlord for the purpose of executing the Tenant's Work including, but not limited to, installing furniture, fixtures, and equipment.

ARTICLE 4
Rent

4.01 Basic Rent.

Tenant shall pay Landlord for the Premises, without offset or deduction and without previous demand therefor, except as expressly set forth herein, the Basic Rent as annual rent for each Lease Year. Basic Rent shall be paid in equal monthly installments in advance on the first day of each calendar month during the Lease Term. The first installment of Basic Rent shall be upon lease execution. Basic Rent for partial months at the beginning or end of the Lease Term shall be pro-rated.

4.02 Computation of Basic Rent.

The Basic Rent for each Lease Year shall be stated in Article 1.01 hereof.

Basic Rent shall be exclusive of (and in addition to) amounts due hereunder for Taxes, Operating Expenses and Estimated Cost of Electrical Service.

4.03 Annual Adjustment of Basic Rent. In accordance with the Rent schedule stated in Section 1.

ARTICLE 5
Use of Premises

5.01 Use Restricted.

The Premises may be used for the Permitted Uses and for no other purpose. No improvements may be made in or to the Premises except as otherwise provided in this Lease.

5.02 Rules and Regulations.

Tenant shall comply with the reasonable Rules and Regulations established from time to time by Landlord, provided such rules and regulations shall not impact Tenant's use of the Premises for the Permitted Uses. Landlord shall not be liable to Tenant for (a) the failure of other tenants to comply with such Rules and Regulations, (b) the failure of other tenants to comply with any term or provision of their respective leases or (c) any nuisance or wrongful, negligent, improper, offensive or unlawful act or omission of any such other tenant.

ARTICLE 6

Taxes; Operating Expenses;
Estimated Cost of Electrical Services

6.01 Expenses and Taxes.

If with respect to any Calendar Year, Tenant's Share of (a) Operating Expenses exceed the Adjusted Operating Expense Base or (b) Taxes exceed the Adjusted Tax Base (whether as the result of an increase in rate or assessment or both), Tenant shall pay to Landlord the amount of each such excess. Any amount due with respect to this Section 6.01 shall be due on the date which is thirty (30) days after receipt by the Tenant of the statement described in Section 6.02 hereof.

6.02 Annual Statement of Additional Rent Due.

Landlord shall render to Tenant a statement, showing (i) for the Calendar Year so indicated (a) Taxes and (b) Operating Expenses and (ii) for the then current Calendar Year, an estimate for (a) Operating Expenses (b) Taxes and (c) Tenant's obligation under Section 6.01.

6.03 Monthly Payments of Additional Rent.

Tenant shall pay to Landlord in advance for each calendar month of the Lease Term falling between receipt by Tenant of the statement described in Section 6.02 and receipt by Tenant of the next such statement, as Additional Rent an amount equal to 1/12th of Tenant's estimated obligation under Section 6.01 shown thereon. The amount due under this Section 6.03 shall be paid with Tenant's monthly payments of Basic Rent and shall be credited by Landlord to Tenant's obligations under Section 6.01. If the total amount paid hereunder exceeds the amount due under such Section, such excess shall be credited by Landlord against the monthly installments of Additional Rent next falling due or shall be refunded to Tenant upon the expiration or termination of this Lease (unless such expiration or termination is the result of an Event of Default or unless the Term has expired in which case Landlord shall refund such excess to Tenant within 30 days after such amount has been determined).

6.04 Accounting Periods.

Landlord shall have the right from time to time to change the periods of accounting hereunder to any other annual period than a Calendar Year, and upon any such change, all items referred to in this Article 6 shall be appropriately apportioned. In all statements rendered under Section 6.02, amounts for periods partially within and partially without the accounting periods shall be appropriately apportioned, and any items which are not determinable at the time of a statement shall be included therein on the basis of Landlord's estimate and with respect thereof Landlord shall render to Tenant promptly after determination a supplemental statement and appropriate adjustment shall be made according thereto.

6.05 Abatement of Taxes.

Landlord may at any time and from time to time make application to the appropriate Governmental Authority for an abatement of Taxes. If (i) such an application is successful for reasons other than the existence of vacancies in the Building and (ii) Tenant has made any payment in respect of Taxes pursuant to this Article 6 for the period with respect to which the abatement was granted, Landlord shall (a) deduct from the amount of the abatement all reasonable expenses

incurred by it in connection with the application (b) recompute Tenant's obligation with respect to Taxes under Section 6.01 and refund any overpayment to Tenant and (c) retain the balance, if any.

6.06 Audit Right.

Furthermore, Tenant may audit Landlord's Operating Expenses in order to verify the accuracy of the charges provided that:

(i)Tenant has made timely payments, without prejudice to Tenant's position, of Additional Rent when due.

(ii)Such audit will be conducted only during regular business hours at the office where Landlord maintains expense records and only after Tenant gives Landlord fourteen (14) days' notice.

(iii) No audit shall be conducted at any time that Tenant is in default (beyond applicable notice and cure periods) of any of the terms of the Lease.

(iv)Tenant shall deliver to Landlord a copy of the results of such audit within fifteen (15) days of its receipt by Tenant.

(v)No subtenant shall have any right to conduct an audit and no assignee shall conduct an audit for any period during which such assignee was not in possession of the Premises.

(vi)Such audit must be conducted by the Internal Audit Department of the Tenant or by an independent nationally recognized accounting firm that is not being compensated by Tenant on a contingency fee basis.

(vii)The audit must commence within one hundred (120) days (time is of the essence) following the delivery to Tenant of Landlord's statement.

(viii)Tenant must deliver to Landlord a signed confidentiality agreement prepared by Landlord in its reasonable discretion.

If any audit by Tenant reveals that Landlord's statement overstated the Operating Expense Additional Rent charge, then the Landlord promptly shall pay to the Tenant the amount of the Tenant's overpayment with interest at the rate set for in Section 22.06 from the date of overpayment until the date the Landlord reimburses the Tenant for the same. If no such payment is made, the Tenant shall be entitled to credit such amount against the monthly installment(s) of Basic Rent next falling due under this Lease, or, if the Lease Term has expired, such amount shall be promptly refunded by the Landlord to the Tenant. If such audit reveals an overpayment of Operating Expenses by six percent (6%) or more, Landlord shall pay the reasonable out-of-pocket costs of Tenant's audit.

6.07 Intentionally Omitted.

6.08 Late Payment of Rent and Late Charges.

Tenant's failure to pay Rent, Additional Rent, or any other Lease costs when due under this Lease may cause Landlord to incur unanticipated costs. The exact amount of such costs are impractical or extremely difficult to ascertain. Such costs may include, but are not limited to,

processing and accounting charges and late charges that may be imposed on Landlord by any ground lease, mortgage, or deed of trust encumbering the Land or Building.

Therefore, if Landlord does not receive the Rent, Additional Rent, or any other Lease costs in full within five (5) days after written notice that the same is past due, Tenant shall pay Landlord a late charge, which shall constitute liquidated damages, equal to five percent (5%) of each unpaid portion ("Late Charge"), which shall be paid to Landlord together with such Rent, Additional Rent, or other Lease costs then in arrears.

The parties agree that such Late Charge represents a fair and reasonable estimate of the cost Landlord will incur by reason of such late payment.

For each Tenant payment check to Landlord that is returned by a bank for any reason, Tenant shall pay both a Late Charge (if applicable) and a returned check charge ("Returned Check Charge") of an amount equal to that charged by Landlord's bank at the time.

All Late Charges and any Returned Check Charge shall then become Additional Rent and shall be due and payable immediately along with such other Rent, Additional Rent, or other Lease costs then in arrears.

Money paid by Tenant to Landlord shall be applied to Tenant's account in the following order: (i) to any unpaid Additional Rent, including, without limitation, Late Charges, Returned Check Charges, legal fees and/or court costs legally chargeable to Tenant, Operating Expenses and Taxes; and then (ii) to unpaid Basic Rent.

Nothing herein contained shall be construed so as to compel Landlord to accept any payment of Rent, Additional Rent, or other Lease costs in arrears or Late Charge or Returned Check Charge should Landlord elect to apply its rights and remedies available under this Lease or at law or in equity in the case of an Event of Default hereunder by Tenant. Landlord's acceptance of Rent, Additional Rent, or other Lease costs in arrears or Late Charge or Returned Check Charge pursuant to this clause shall not constitute a waiver of Landlord's rights and remedies available under this Lease at law or in equity.

ARTICLE 7
Improvements, Repairs, Additions, Replacements

7.01 Preparation of the Premises.

Except as provided in Exhibit B and C and subject to (i) Landlord's obligation to complete the Landlord's Work and deliver the Premises to Tenant with Building HVAC and all life safety systems in good working order and (ii) Landlord's ongoing obligations for repairs and compliance with the ADA in the Common Areas, the Premises shall be leased in its present "as is" condition as of the date hereof, and Landlord shall have no obligation to perform any work or construction in the Premises to prepare it for Tenant's occupancy.

7.02 Alterations and Improvements.

Except for Tenant’s Work that has been approved by Landlord pursuant to Exhibit B and C, Tenant shall not make alterations or additions to the Premises without Landlord’s prior written approval (which approval shall not be unreasonably withheld, conditioned or delayed) and then only in accordance with plans and specifications therefor first approved by Landlord. Tenant shall not hang shades, curtains, signs, awnings or other materials to or make any change in the appearance of any glass visible from outside of the Premises, add any window treatments of any kind or install furniture visible from outside of the Premises, without Landlord's prior written consent (other than tinting and other window treatments along the glass line), such consent not to be unreasonably withheld, conditioned or delayed. Without limitation, Landlord may withhold approval of any alterations or additions which would delay completion of the Premises or the Building. All alterations and additions shall be part of the Premises unless and until Landlord shall specify the same for removal in a notice delivered to Tenant at the time of Landlord’s consent thereto. All of Tenant's alterations and additions and installation of furnishings shall be coordinated with any work being performed by Landlord and in such manner as to maintain harmonious labor relations and not to damage the Building or the Premises or interfere with Building operation and, except for installation of furnishings, shall be performed by contractors or workmen first approved by Landlord (which approval shall not be unreasonably withheld, conditioned or delayed). Except for work done by or through Landlord, Tenant before its work is started shall: secure all licenses and permits necessary therefor; deliver to Landlord a statement of the names of all its contractors and subcontractors and the estimated cost of all labor and material to be furnished by them; and cause each contractor to carry workmen's compensation insurance in statutory amounts covering all the contractor's and subcontractor's employees and commercial general liability insurance with limits as Landlord may reasonably require, but in no event less than $1,000,000.00 and property damage insurance with limits of not less than $1,000,000.00 and have deductibles of no more than $50,000.00 (all such insurance to be written by companies approved by Landlord and insuring Tenant and Landlord and its managing agent and its mortgagees, as well as the contractors), and to deliver to Landlord certificates of all such insurance. Tenant agrees to pay promptly when due the entire cost of any work done in the Premises by Tenant, its agents, employees or independent contractors, and not to cause or permit any liens therewith to attach to the Premises and to discharge any such liens which may so attach within the time period required under this Lease. All construction work done by Tenant, its agents, employees or independent contractors shall be done in a good and workmanlike manner and in compliance with all Legal Requirements and Insurance Requirements.

Landlord reserves the right to require that Tenant remove any Alterations and/or Tenant’s Systems installed by or for Tenant within or serving the Premises upon the expiration or earlier termination of this Lease. Such notice to Tenant shall occur at least six (6) months prior to the expiration of the Term of this Lease. If Tenant fails to remove any Alterations and/or Tenant’s Systems so required, such failure shall be an Event of Default hereunder, and Landlord shall have all rights and remedies available under this Lease, at law or in equity, including the right to remove any Alterations and/or Tenant’s Systems at Tenant’s expense. Tenant acknowledges and agrees that any Alterations and/or Tenant’s Systems installed by or for Tenant within or serving the Premises shall be the property of Tenant during the Term. Any Alterations and/or Tenant’s Systems not removed by Tenant shall, at Landlord’s option, become the property of Landlord (without payment by Landlord) at the expiration or earlier termination of this Lease.

Tenant may make cosmetic alterations or improvements (i.e., painting, carpeting, flooring, etc.) regardless of cost and any other non-structural alterations, additions or improvements having a cost, in each instance, of $50,000.00 or less, without Landlord's prior consent and Tenant may make non-structural alterations, additions or improvements having a cost, in each instance, in excess of $50,000.00, with Landlord's prior written consent, which consent shall not be unreasonably withheld or delayed. Any structural alterations, additions or improvements shall become part of the Premises and the property of Landlord. Any other alterations, additions or improvements which are removable shall remain the property of Tenant and may be removed by Tenant upon the termination of this Lease.

7.03 Maintenance.

Except for Landlord's obligations under Section 8.01, Tenant shall, at all times during the Lease Term, and at its own cost and expense, (i) keep and maintain the interior of the Premises in good repair and condition (ordinary wear and tear and damage by fire or casualty only excepted), (ii) use all reasonable precautions to prevent waste, damage or injury thereto and (iii) maintain all systems and equipment that exclusively serves the Premises.

7.04 Redelivery.

On the Lease Termination Date, without limiting its other obligations under this Lease, Tenant shall surrender all keys to the Premises, remove Tenant's signage and remove all of its trade fixtures which in Tenant's sole discretion, it elects to remove and restore any damage caused by such removal. Tenant shall, subject to the provisions of Articles 17 and 18 hereof, surrender the Premises to Landlord broom clean and in good condition and repair with ordinary wear and tear and damage by fire or casualty only excepted. Any property not so removed shall be deemed abandoned and may be removed and disposed of by Landlord in such manner as it shall determine.

ARTICLE 8
Building Services

8.01 Building Services; Maintenance.

Landlord shall furnish, or cause to be furnished, during the Lease Term the Basic Services.

Subject to Articles 17 and 18, Landlord shall maintain the Common Areas, exterior walls (exclusive of glass and doors and exclusive of the interior surface of the exterior walls, all of which Tenant shall maintain and repair), roof, foundation, structural supports of the Building and the heating, plumbing, electrical, air-conditioning and mechanical and all other Building systems.

8.02 Other Janitors.

No persons shall be employed by Tenant to do janitorial work in the Premises other than the lab areas and no persons other than the janitors of the Building shall clean the office areas of the Premises unless Landlord shall give its written consent thereto. Any person employed by Tenant with Landlord's consent to do janitorial work shall, while in the Building, either inside or outside the Premises, be subject to and under the control and direction of the superintendent of the Building (but not as agent or servant of said superintendent or of Landlord).

8.03 Additional Services.

Tenant will pay the Landlord a reasonable charge for any extra cleaning of the Premises required because of the carelessness or indifference of Tenant and for any Additional Services rendered at the request of Tenant. If the cost of cleaning the Premises shall be increased due to the installation in the Premises, at Tenant's request, of any unique or special materials, finish or equipment, Tenant shall pay the Landlord an amount equal to such increase in cost. All charges for Additional Services shall be due and payable within ten (10) days of the date on which they are billed.

8.04 Limitations on Landlord's Liability.

Landlord shall not be liable in damages, and not in default hereunder, for any failure or delay in complying with its obligations hereunder, including, without limitation, furnishing electricity, any Basic Service or Additional Service, when such failure or delay is occasioned by Force Majeure or by the act or Default of Tenant. No such failure or delay shall be held or pleaded as eviction or disturbance in any manner whatsoever of Tenant's possession or give Tenant any right to terminate this Lease or give rise to any claim for set-off or any abatement of Rent of any of Tenant's obligations under this Lease. Landlord's failure to furnish, or any interruption or termination of, services due to the application of Laws, the failure of any equipment, the performance of repairs, improvements or alterations, or the occurrence of any event or cause beyond the reasonable control of Landlord (a "Service Failure") shall not render Landlord liable to Tenant, constitute a constructive eviction of Tenant, give rise to an abatement of Rent, nor relieve Tenant from the obligation to fulfill any covenant or agreement. However, if the Premises, or a material portion of the Premises, is made untenantable for a period in excess of five (5) consecutive Business Days as a result of the Service Failure, then Tenant, as its sole remedy, shall be entitled to receive an abatement of Rent payable hereunder during the period beginning on the sixth (6^{th}) consecutive Business Day of the Service Failure and ending on the day the service has been restored. If the entire Premises has not been rendered untenantable by the Service Failure, the amount of the abatement that Tenant is entitled to receive shall be prorated based upon the percentage of the Premises rendered untenantable and not used by Tenant.

8.05 Electric Service.

Electricity is separately metered for the Premises, therefore, Tenant, beginning on the Term Commencement Date and at its expense, shall obtain electricity from such source or sources as Landlord shall designate as the electricity source or sources for the Building, provided Tenant shall have the right, from time to time after notice to Landlord, to elect to obtain electrical services from a provider of its choosing.

ARTICLE 9
Tenant's Particular Covenants

9.01 Pay Rent.

Tenant shall pay when due all Rent and all charges for utility services rendered to the Premises not included in Rent and, as further Additional Rent, all charges charged by Landlord for Additional Services provided at Tenant's request.

9.02Occupancy of the Premises.

Tenant shall occupy the Premises from the Term Commencement Date for the Permitted Uses only. Tenant shall not (i) injure or deface the Premises or the Building, (ii) install any sign in or on any window, or Common Area, (iii) permit in the Premises any flammable fluids or chemicals not reasonably related to the Permitted Uses nor (iv) permit nuisance or any use thereof which is contrary to any Legal Requirement or Insurance Requirement or liable to render necessary any alteration or addition to the Building.

Tenant shall not permit any noise, vibration or odor to emit from the Premises which in Landlord's reasonable discretion is offensive or inappropriate for a first class office and laboratory Building with the Permitted Uses.

9.03Safety.

Tenant shall keep the Premises equipped with all safety appliances required by Legal Requirements or Insurance Requirements because of any specific use made by Tenant. Tenant shall procure all Authorizations so required because of such use and, if requested by Landlord, shall do any work so required because of such use, it being understood that the foregoing provision shall not be construed to broaden in any way the Permitted Uses. Any storage, delivery and removal of materials shall be done in such a manner so as not to unreasonably interfere with other tenants of the Building.

9.04Equipment.

Tenant shall not place a load upon the floor of the Premises exceeding the live load for which the floor has been designed for fifty (50) pounds per square foot; and shall not move any safe or other heavy equipment in, about or out of the Premises except in such a manner and at such a time as Landlord shall in each instance authorize, such authorization not to be unreasonably withheld, delayed or conditioned. Tenant shall isolate and maintain all of Tenant's machines and mechanical equipment which cause or may cause air-borne or structure-borne vibration or noise, whether or not it may be transmitted to any other premises so as to eliminate such vibration or noise.

9.05Electrical Equipment.

Except with respect to the laboratory space in the Premises and the associated roof top equipment, Tenant shall not, without prior written notice to Landlord in each instance (i) connect to the Building electric distribution system anything other than normal office equipment or (ii) operate such equipment on a regular basis beyond normal Building operating hours. Tenant's use of electrical energy in the Premises shall not at any time exceed the capacity of any of the electrical conductors or equipment in or otherwise serving the Premises. Tenant shall have the right (i) to connect to the main panel and submeter dedicated HVAC in the lab portions at all times and (ii) to install its own dedicated e-power unit to be mounted to the roof, subject to Landlord prior approval of placement and method of installation, such approval shall not be unreasonably withheld, delayed or conditioned.

9.06Pay Taxes.

Tenant shall pay promptly when due all Taxes upon personal property (including, without limitation, fixtures and equipment) in the Premises to whomsoever assessed.

ARTICLE 10
Requirements of Public Authority

10.01 Legal Requirements.

Tenant shall, at its own cost and expense, promptly observe and comply with all Legal Requirements. Tenant shall pay all costs, expenses, liabilities, losses, damages, fines, penalties, claims and demands that may in any manner arise out of or be imposed because of the failure of Tenant to comply with the covenants of this Article 10. The Landlord shall not be responsible or liable for any loss or interruption of Tenant's business, or any costs of compliance, caused by the enforcement of any Legal Requirements which are related to Tenant's use of the Premises or the Common Areas, provided that if Tenant is prohibited from using the Premises for the Permitted Uses as a result of any Legal Requirements, Tenant may terminate this Lease upon 30 days' notice to Landlord. Notwithstanding the foregoing or any other provision of this Lease, however, Tenant shall not be responsible for compliance with any such Legal Requirements or the like requiring (a) structural repairs or modifications; or (b) repairs or modifications to the utility or building service equipment; or (c) installation of new building service equipment, such as fire detection or suppression equipment, unless such repairs, modifications, or installations shall (i) be due to Tenant's particular manner of use of the Premises for laboratory uses, or (ii) be due to the negligence or willful misconduct of Tenant or any agent, employee, or contractor of Tenant.

Tenant shall not dump, flush, or in any way introduce any Hazardous Substances or any other toxic substances into the septic, sewage or other waste disposal system or generate, store or dispose of Hazardous Substances in or on the Premises or the Land, or dispose of Hazardous Substances from the Premises or the Land to any other location except in the ordinary course of Tenant's business and then only in compliance with the Resource Conservation and Recovery Act of 1976, as amended, 42 U.S.C.§6901 et seq., the Massachusetts Hazardous Waste Management Act, M.G.L. c.21C., as amended, the Massachusetts Oil and Hazardous Material Release Prevention and Response Act, M.G.L. c.21E, as amended, and all other applicable codes, regulations, ordinances and laws. Tenant shall notify Landlord of any incident which would require the filing of a notice under M.G.L. c.21E and shall comply with the orders and regulations of all governmental authorities with respect to zoning, building, fire, health and other codes, regulations, ordinances or laws applicable to the Premises or the Land. "Hazardous Substances" as used in this Section shall mean "hazardous substances" as defined in the Comprehensive Environmental Response Compensation and Liability Act of 1980, as amended, 42 U.S.C. §9601 and regulations adopted pursuant to such Act. Landlord hereby acknowledges that Tenant will have a pH neutralization system and will discharge wastewater from the Premises into the sewer system.

Landlord hereby agrees to defend, indemnify and hold Tenant harmless from and against any and all loss, cost, damage, claim or expense (including legal fees) incurred in connection with or arising out of or relating in any way to the presence of Hazardous Substances as of the date hereof in or on the Land or the Building.

Tenant will provide Landlord, from time to time upon Landlord’s request, with all reasonable records and information regarding any Hazardous Substance maintained on the Premises by Tenant.

Landlord and Tenant agree as follows with respect to the existence or use of "Hazardous Material" in or on the Premises, the Building.

Tenant, at its sole cost and expense, shall comply with the Emergency Planning and Community Right to Know Act (EPCRTKA) 42 U.S.C. § 11001-11050, and all other laws, statutes, ordinances, rules and regulations of any local, state or federal governmental authority having jurisdiction concerning environmental, health and safety matters (collectively, "Environmental Laws"), including, but not limited to, any discharge into the air, surface, water, sewers, soil or groundwater of any Hazardous Material (as defined in Article 29.11(c)), whether within or outside the Premises within the Complex. For purpose of this Lease, the term “Complex” shall mean the buildings located at 120 Presidential Way and 150 Presidential Way in Woburn, MA. Tenant shall comply with all terms, conditions and guidelines contained in the MWRA permit applicable to the Premises and agrees to further acknowledge such agreement to so comply in writing upon request of Landlord. Notwithstanding any provision of this Lease to the contrary, nothing contained in this Lease requires, or shall be construed to require, Tenant to incur any liability related to or arising from environmental conditions (i) for which the Landlord is responsible pursuant to the terms of this Lease, or (ii) which existed within the Premises or the Complex prior to the date Tenant takes possession of the Premises.

Tenant shall not cause or permit any Hazardous Material to be brought upon, kept or used in or about the Premises or otherwise in the Complex by Tenant, its agents, employees, contractors or invitees, without the prior written consent of Landlord, except for Hazardous Materials which are typically used in the operation of offices or laboratories, provided that such materials are stored, used and disposed of in strict compliance with all applicable Environmental Laws and with good scientific and medical practice. Within twenty (20) days of Landlord’s request, Tenant shall provide Landlord with a list of all Hazardous Materials, including quantities used and such other information as Landlord may reasonably request, used by Tenant in the Premises or otherwise in the Complex. Tenant represents that the list attached hereto as Exhibit J is a complete list of all Hazardous Materials and quantities that may be used by Tenant in the Premises as of the Execution Date, which list Tenant may supplement or revise during the Term. Notwithstanding the foregoing, with respect to any of Tenant's Hazardous Material which Tenant does not properly handle, store or dispose of in compliance with all applicable Environmental Laws and good scientific and medical practice, Tenant shall, upon written notice from Landlord, no longer have the right to bring such material into the Premises, Building of which the Premises is a part until Tenant has demonstrated, to Landlord's reasonable satisfaction, that Tenant has implemented programs to thereafter properly handle, store or dispose of such material.

As used herein, the term "Hazardous Material" means any hazardous or toxic substance, material or waste or petroleum derivative which is or becomes regulated by any Environmental Law, specifically including live organisms, viruses and fungi, medical waste, and so-called “biohazard” materials. The term "Hazardous Material" includes, without limitation, any material or substance which is (i) designated as a "hazardous substance" pursuant to Section 1311 of the Federal Water Pollution Control Act (33 U.S.C. Section 1317), (ii) defined as a “hazardous waste” pursuant to

Section 1004 of the Federal Resource Conservation and Recovery Act, 42 U.S.C. Section 6901 et seq. (42 U.S.C. Section 6903), (iii) defined as a "hazardous substance" pursuant to Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act, 42 U.S.C. Section 9601 et seq. (42 U.S.C. Section 9601), (iv) defined as "hazardous substance" or "oil" under Chapter 21E of the General Laws of Massachusetts, or (v) a so-called “biohazard” or medical waste, or is contaminated with blood or other bodily fluids; and "Environmental Laws" include, without limitation, the laws listed in the preceding clauses (i) through (iv).

Any increase in the premium for necessary insurance on the Premises or the Building which arises from Tenant's use and/or storage of these Hazardous Materials shall be solely at Tenant's expense. Tenant shall procure and maintain at its sole expense such additional insurance as may be necessary to comply with any requirement of any federal, state or local government agency with jurisdiction. Tenant hereby covenants and agrees to indemnify, defend and hold Landlord harmless from any and all claims, judgments, damages, penalties, fines, costs, liabilities or losses (collectively "Losses") which Landlord may reasonably incur arising out of contamination of real estate, the Building or other property not a part of the Premises, which contamination arises as a result of: (i) the presence of Hazardous Material in the Premises, the presence of which is caused or permitted by Tenant, or (ii) from a breach by Tenant of its obligations under this Section 10.01. This indemnification of Landlord by Tenant includes, without limitation, reasonable costs incurred in connection with any investigation of site conditions or any cleanup, remedial, removal or restoration work required by any federal, state or local governmental agency or political subdivision because of Hazardous Material present in the soil or ground water on or under the Premises caused by Tenant or its agents, employees, contractors or invitees. The indemnification and hold harmless obligations of Tenant under this Section 10.01 shall survive any termination of this Lease. Without limiting the foregoing, if the presence of any Hazardous Material in the Building or otherwise caused or permitted by Tenant results in any contamination of the Premises, Tenant shall promptly take all actions at its sole expense as are necessary to return the Premises to a condition which complies with all Environmental Laws; provided that Landlord's approval of such actions shall first be obtained, which approval shall not be unreasonably withheld, conditioned or delayed so long as such actions, in Landlord's reasonable discretion, would not potentially have any materially adverse long-term or short-term effect on the Premises, and, in any event, Landlord shall not withhold its approval of any proposed actions which are required by applicable Environmental Laws.

On or before the date that Tenant, and anyone claiming by, through or under Tenant, vacates the Premises, and immediately prior to the time that Tenant delivers the Premises to Landlord, Tenant shall cause the Premises to be decommissioned in accordance with the regulations of the U.S. Nuclear Regulatory Commission and/or the Massachusetts Department of Public Health for the control of radiation, cause the Premises to be released for unrestricted use by the Radiation Control Program of the Massachusetts Department of Public Health for the control of radiation, and deliver to Landlord the report of a certified industrial hygienist stating that he or she has examined the Premises (including visual inspection, Geiger counter evaluation and airborne and surface monitoring) and found no evidence that such portion contains Hazardous Materials, as defined in

this Article, or is otherwise in violation of any Environmental Law, as defined in this Article hereof.

Provide to Landlord a copy of its most current chemical waste removal manifest and a certification from Tenant executed by an officer of Tenant that no Hazardous Materials or other potentially dangerous or harmful chemicals brought onto the Premises from and after the date that Tenant first took occupancy of the Premises remain in the Premises.

Landlord hereby agrees that the maximum allowable quantities of Hazardous Materials available for the Building shall be allocated in their entirety to Tenant. Notwithstanding any provision of this Lease to the contrary, nothing in this paragraph shall be read or deemed to prohibit Landlord from entering into new leases with laboratory tenants or from creating additional control areas in the Building to facilitate other laboratory leases, provided (i) Landlord shall create any additional control areas necessary for such laboratory tenants hazardous materials storage needs, (ii) in no event shall Tenant have any obligation to perform any work or pay any costs (whether as Operating Expenses or otherwise) associated with creating any such additional control areas or arising from the introduction of other laboratory tenants into the Building including, without limitation, costs of satisfying any fire separation requirements, and (iii) there shall be no reduction or diminishment of the allowable quantities of Hazardous Materials that Tenant may use or store within the Building.

10.02 Contests.

Tenant shall have the right to contest by appropriate legal proceedings diligently conducted in good faith, in the name of the Tenant or Landlord (if legally required), or both (if legally required), without cost, expense, liability or damage to Landlord, the validity or application of any Legal Requirement and, if compliance with any of the terms of any such Legal Requirement may legally be delayed pending the prosecution of any such proceeding, Tenant may delay such compliance therewith until the final determination of such proceeding.

ARTICLE 11
Covenant Against Liens

11.01 Mechanics' Liens.

Landlord's right, title and interest in the Premises, the Land or the Building shall not be subject to or liable for liens of mechanics or materialmen for work done on behalf of Tenant in connection with improvements to the Premises. Notwithstanding such restriction, if because of any act or omission of Tenant, any mechanics' lien or other lien, charge or order for payment of money shall be filed against any portion of the Premises or the Land or the Building, Tenant shall, at its own cost and expense, cause the same to be discharged of record within fifteen (15) days after the filing thereof.

11.02 Right to Discharge.

Without otherwise limiting any other remedy of Landlord for default hereunder, if Tenant shall fail to cause such liens to be discharged of record within the aforesaid fifteen (15) day period,

then Landlord shall have the right to cause the same to be discharged. All reasonable amounts paid by Landlord to cause such liens to be discharged shall constitute Additional Rent.

ARTICLE 12
Access to Premises

12.01 Access.

Landlord or Landlord's agents and designees shall have the right, but not the obligation, to enter upon the Premises at all reasonable times during ordinary business hours and after reasonable prior notice to Tenant to examine same and to exhibit the Premises to prospective purchasers, mortgagees, tenants or other persons or agents as Landlord shall designate from time to time, though exhibition to tenants shall only occur during the last 12 months of the Term; provided that, in all events those accessing the Tenant's Premises shall be accompanied by a Tenant representative.

ARTICLE 13
Assignment and Subletting: Occupancy Arrangements

13.01 Subletting and Assignment.

Tenant shall not enter into any Occupancy Arrangement, either voluntarily or by operation of law without the prior consent of Landlord, which consent will not be unreasonably withheld, conditioned or delayed. Without limiting the generality of the foregoing, in no event shall Tenant enter sublet all or any part of the Premises or to assign this Lease, offer to so sublet or assign or so sublet or assign to any tenant or occupant of the Building or to any party with whom Landlord is then negotiating with respect to space in the Building as evidenced by a written proposal.

If Tenant intends to enter into an Occupancy Arrangement, Tenant shall so notify Landlord in writing, stating the name of (and providing a financial statement with respect to) the Person whom Tenant intends to enter into such Arrangement, the exact terms of the Occupancy Arrangement and a precise description of the portion of the Premises intended to be subject thereto. Within thirty (30) days of receipt of such writing, Landlord shall either consent to such Occupancy Arrangement or deny consent to such Occupancy Arrangement. The Landlord shall not be deemed to be unreasonable in denying its consent to any proposed assignment or subletting by the Tenant based on any of the following factors:

(a) The business of the proposed tenant is not consistent with the image and character which the Landlord desires to promote for the Building; and

(b) The proposed assignment or subletting could adversely affect the ability of the Landlord and its affiliates to lease space in the Building including leasing space to any proposed assignee or subtenant; and

(c) The credit worthiness of the proposed tenant is unsatisfactory to the Landlord, as the Landlord may determine in its reasonable discretion.

If the Landlord consents to such Occupancy Arrangement, Tenant shall (i) enter into such Arrangement on the exact terms described to Landlord within thirty (30) days of Landlord's

consent or comply again with the terms of this Section and (ii) remain liable for the payment and performance of the terms and covenants of this Lease. If Tenant enters into such an Occupancy Arrangement, Tenant shall pay to Landlord when received 50% of the excess, if any, of amounts received in respect of such Occupancy Arrangement over the Rent, after deducting Tenant's costs of brokerage, legal fees, tenant improvements and any rent concessions. For the purpose of the preceding sentence, amounts received by Tenant in respect of such Occupancy Arrangement shall be deemed to include any sums paid for the sale, rental or use of any of Tenant's personal property (in the case of a sale only, reduced by Tenant's depreciated basis thereof for federal income tax purposes).

If Tenant's stock is not publicly held, the provisions of this Section 13.01 shall apply to a transfer (by one or more transfers) of a majority of the stock or other ownership interests of Tenant as if Tenant had entered into an Occupancy Arrangement. Such provisions shall not apply and Tenant shall have the right to enter into an Occupancy Arrangement in connection with any transactions with an entity into or with which Tenant is merged or consolidated or to which substantially all of Tenant's assets are transferred or to any entity which controls or is controlled by Tenant or is under common control with Tenant, provided that in any of such events (i) the successor to Tenant has a tangible net worth computed in accordance with generally accounting principles at least equal to the tangible net worth of Tenant immediately prior to such merger, consolidation or transfer, (ii) proof satisfactory to Landlord of such tangible net worth shall have been delivered to Landlord at least ten (10) days prior to the effective date of any such transaction, and (iii) the assignee agrees directly with Landlord, by written instrument in form reasonably satisfactory to Landlord, to be bound by all the obligations of Tenant hereunder including, without limitation, the covenant against further assignment or subletting.

ARTICLE 14
Indemnity

14.01 Tenant's Indemnity.

To the fullest extent permitted by law, Tenant shall indemnify and hold harmless Landlord from and against any and all liability, damage, penalties or judgments and from and against any claims, actions, proceedings and expenses and costs in connection therewith, including reasonable counsel fees, arising from injury to person or property sustained by anyone in and about the Building or the Premises or the Land by reason of an act or omission of Tenant, or Tenant's officers, agents, servants, employees, contractors, sublessees or invitees. Tenant shall, at its own cost and expense, defend any and all suits or actions (just or unjust) in which Landlord may be impleaded with others upon any such above mentioned matter, claim or claims, except as may result from the acts as set forth in Section 14.02. All merchandise, furniture, fixtures and property of every kind, nature and description of Tenant or Tenant's employees, agents, contractors, invitees, visitors, or guests which may be in or upon the Premises, the Land or the Building during the Lease Term shall be at the sole risk and hazard of Tenant, and if the whole or any part thereof shall be damaged, destroyed, stolen or removed by reason of any cause or reason whatsoever, other than the negligence or willful misconduct of Landlord, no part of said damage or loss shall be charged to or borne by Landlord.

14.02 Landlord's Liability.

Except for the negligence or willful misconduct of Landlord or of its officers, agents, servants, employees or contractors, Landlord shall not be responsible or liable for any damage or injury to any property, fixtures, buildings or improvements, or to any person or persons, at any time in the Premises, including any damage or injury to Tenant or to any of Tenant's officers, agents, servants, employees, contractors, invitees, customers or sublessees. To the fullest extent permitted by law, Landlord shall indemnify and hold harmless Landlord from and against any and all liability, damage, penalties or judgments and from and against any claims, actions, proceedings and expenses and costs in connection therewith, including reasonable counsel fees, arising from the willful acts or negligence of Landlord or the willful acts or negligence of its officers, agents, servants, employees or contractors.

ARTICLE 15
Insurance

15.01 Liability Insurance.

Tenant shall maintain, at its expense, in force during the Lease Term, commercial general liability insurance in a good and solvent insurance company or companies licensed to do business in the Commonwealth of Massachusetts, selected by Tenant, and reasonably satisfactory to Landlord, and in an amount reasonably required by Landlord from time to time but in any event not less than Five Million Dollars ($5,000,000.00) with respect to injury or death to any one person and Five Million Dollars ($5,000,000.00) with respect to injury or death to more than one person in any one accident or other occurrence and Five Million Dollars ($5,000,000.00) with respect to damage to property. Such policy or policies shall include Landlord and Landlord’s managing agent and mortgagees as additional insureds and have deductibles of no more than $50,000.00.

Tenant shall also maintain in force during the Lease Term worker’s compensation insurance with statutory limits covering all of Tenant’s employees working at the Premises.

15.02 Casualty Insurance.

Tenant shall cause its improvements to the Premises to be insured for the benefit of Landlord and Tenant, as their respective interests may appear, against loss or damage under all risk coverage satisfactory to Landlord in an amount equal to the replacement value thereof. Certificates thereof shall be delivered to Landlord. Landlord shall not carry any insurance concurrent in coverage and contributing in the event of loss with any insurance required to be furnished by Tenant hereunder if the effect of such separate insurance would be to reduce the protection or the payment to be made under Tenant’s insurance.

15.03 Certificates.

Tenant agrees to deliver to Landlord certificates of the insurance required under Sections 15.01 and 15.02 as of the date hereof and thereafter not less than thirty (30) days prior to the expiration of any such policy. Such insurance shall not be cancelable without thirty (30) days’ written notice to Landlord.

15.04 **Landlord’s Insurance.** Landlord agrees to maintain in full force from the date upon which Tenant first enters the Premises for any reason, throughout the Term, a policy of insurance

upon the Building insuring against all risks of physical loss or damage under an All Risk coverage endorsement in an amount at least equal to the full replacement value of the property insured, with an Agreed Amount endorsement to satisfy co-insurance requirements, as well as insurance against breakdown of boilers and other machinery as customarily insured against. Landlord shall supply to Tenant from time to time upon request of Tenant certificates of all such insurance issued by or on behalf of the insurers named therein by a duly authorized agent.

ARTICLE 16
Waiver of Subrogation

16.01 Waiver of Subrogation.

All property insurance policies carried by either party covering the Premises, including but not limited to contents, fire and casualty insurance, shall expressly waive any right on the part of the insurer to make any claim against the other party. The parties hereto agree that their policies will include such waiver clause or endorsement.

16.02 Waiver of Rights.

Each Landlord and Tenant, on behalf of itself and its insurers, hereby waives all claims, causes of action and rights of recovery against the other and the other's respective partners, agents, officers and employees, for any damage to or destruction of property or business which shall occur on or about the Land or the Building and shall result from any of the perils insured under any and all policies of insurance maintained by the waiving party, regardless of cause, including the negligence and intentional wrongdoing of either party and their respective agents, officers and employees but only to the extent of recovery, if any under such policy or policies of insurance; provided however, that this waiver shall be ineffective in the event any such insurer would be relieved from the obligation to make payment pursuant to a policy of insurance by reason of this waiver.

ARTICLE 17
Damage or Destruction

17.01 Substantial Damage.

If the Building or any part thereof shall be damaged by fire or other casualty to the extent that substantial alteration or reconstruction of the Building shall, in Landlord's reasonable opinion, be required (whether or not the Premises shall have been damaged) or if all or any portion of the insurance proceeds are applied to the mortgage debt or if the net insurance proceeds available to Landlord are insufficient to restore, Landlord may, at its option, terminate this Lease by notifying Tenant in writing of such termination within sixty (60) days after the date of such damage. If this Lease is so terminated, Rent shall be abated as of the date of such damage. If the Premises are (a) materially damaged by fire or other casualty during the last twelve (12) months of the Term and Tenant has not exercised its Term extension rights under this Lease, or (b) materially damaged by fire or other casualty and not restored (including restoration of any Landlord's Work) within one hundred eighty (180) days after the date of such fire or other casualty, then Tenant shall have the right, exercisable by notice to Landlord delivered within thirty (30) days after the date of such fire or other casualty (with respect to clause (a) above) or at any time after expiration of such one

hundred eighty (180) day period while failure to restore the Premises and the Landlord's Work persists (with respect to clause (b) above), to terminate this Lease, effective as of the date of delivery of such notice.

17.02 Restoration.

If Landlord does not terminate this Lease pursuant to Section 17.01, Landlord shall, after receipt by Landlord of the Proceeds payable in respect of such fire or other casualty, proceed with reasonable diligence to repair and restore the Building (subject to Force Majeure) to substantially the same condition in which it was immediately prior to the occurrence of the casualty. Landlord may, but shall not be required to, repair or restore any alterations or improvements made by Tenant, and, if Landlord elects to do so, Tenant shall make available to Landlord all insurance proceeds relating thereto; provided, however, in all events Tenant shall be responsible for any specialty construction related to non-office portions of the Premises and shall be entitled to the insurance proceeds reasonably allocated for such work. Landlord shall not be required to rebuild, repair, or replace any part of Tenant's furniture, furnishings or fixtures or equipment, which shall be a Tenant responsibility. Landlord shall not be liable for any inconvenience or annoyance to Tenant or injury to the business of Tenant resulting in any way from such damage or the repair thereof, except that, Landlord shall allow Tenant a proportionate abatement of Rent during the time and to the extent the Premises are unfit for occupancy.

ARTICLE 18
Eminent Domain

18.01 Total Taking.

If the Premises or the Building should be the subject of a Total Taking, then this Lease shall terminate as of the date when physical possession of the Building or the Premises is taken by the condemning authority.

18.02 Partial Taking.

If there shall occur a Partial Taking, Rent shall be abated by an amount representing that part of the Rent properly allocable to the portion of the Premises so taken and Landlord shall, at Landlord's sole expense, restore and reconstruct the Building (to the extent of the net proceeds made available to Landlord) and the Premises to substantially their former condition to the extent that the same, in Landlord's judgment, may be feasible. The Landlord shall have no liability for interruption of Tenant's business to the extent caused by any such Partial Taking.

18.03. Awards and Proceeds.

All Proceeds payable in respect of a Taking shall be the property of Landlord. Tenant hereby assigns to Landlord all rights of Tenant in or to such Proceeds, provided that Tenant shall be entitled to separately petition the condemning authority for a separate award for its moving expenses and trade fixtures but only if such a separate award will not diminish the amount of Proceeds payable to Landlord.

ARTICLE 19
Quiet Enjoyment

19.01 Landlord's Covenant.

Provided that an Event of Default has not occurred and is not then continuing, Tenant shall quietly have and enjoy the Premises during the Lease Term, without hindrance or molestation from any Person lawfully claiming by, through or under Landlord.

19.02 Superiority of Lease: Option to Subordinate.

At any time and from time to time, Landlord shall have the option to subordinate this Lease to any mortgage of the Premises provided that the holder of record thereof enters into a non-disturbance agreement with Tenant in such holder's customary and commercially reasonable form or, if specified by Landlord, in the form of Exhibit G hereto. Tenant agrees to execute and deliver any reasonably appropriate instruments necessary to carry out the agreements contained in this Section 19.02.

19.03 Notice to Mortgagee.

No act or failure to act on the part of Landlord which would entitle Tenant under the terms of this Lease, or by law, to be relieved of Tenant's obligations hereunder or to terminate this Lease, shall result in a release or termination of such obligations or a termination of this Lease unless (i) Tenant shall have first given written notice of Landlord's act or failure to act to Landlord's mortgagees of record, if any, specifying the act or failure to act on the part of Landlord which could or would give rise to Tenant's rights, and (ii) such mortgagees, after receipt of such notice, have had the opportunity to cure such default within a reasonable time thereafter; but nothing contained in this Section 19.03 shall be deemed to impose any obligation on any such mortgagees to correct or cure any such condition. "Reasonable time" as used above shall mean a period of not less than thirty (30) Business Days and shall include (but not be limited to) a reasonable time to obtain possession of the Building if the mortgagee elects to do so and a reasonable time to correct or cure the condition if such condition is determined to exist.

19.04 Other Provisions Regarding Mortgagees.

If this Lease or the Rent due hereunder is assigned to a mortgagee as collateral security for a loan, no such mortgagee shall be deemed to have assumed any of Landlord's obligations hereunder solely as a result of said assignment. A mortgagee to whom this Lease has been so assigned shall be deemed to have assumed such obligations only if (i) by the terms of the instrument of assignment such mortgagee specifically elects to assume such obligations or (ii) such mortgagee has (a) foreclosed its mortgage, (b) accepted a deed in lieu thereof, or (c) taken possession of the Premises by entry or otherwise. Even if such mortgagee assumes the obligations of Landlord hereunder, (i) any such obligation under Section 24.01 to return the Security Deposit to the Tenant shall be limited to the amount actually received by the mortgagee with respect thereto, and (ii) such mortgagee will be liable for breaches of any of Landlord's obligations hereunder only to the extent such breaches occur during the period of ownership by the mortgagee after foreclosure (or any conveyance by a deed in lieu thereof), all as set forth in Section 25.09 hereof. Tenant shall from time to time, at the request of Landlord or any of Landlord's mortgagees, provide Landlord and such mortgagee with financial information pertaining to Tenant as Landlord or such mortgagee may reasonably request.

ARTICLE 20
Defaults; Events of Default

20.01 Defaults.

The following shall, if any requirement for notice or lapse of time or both has not been met, constitute Defaults, and, if such requirement for notice or lapse of time have been met, constitute Events of Default hereunder:

(1) Occurrence of any event set forth in Article 21 hereof;

(2) The failure of Tenant to pay Rent when the same shall be due and payable and the continuance of such failure for a period of five (5) days after receipt by Tenant of notice in writing from Landlord specifying such failure;

(3) The failure of Tenant to observe any covenant made by it in Sections 13.01, 15.01 and 25.03 hereof, which remains uncured for twenty (20) days after written notice from Landlord;

(4) The failure of Tenant to keep, observe or perform any of the other covenants, conditions and agreements herein contained on Tenant's part to be kept, observed or performed and the continuance of such failure without the curing of same for a period of twenty (20) days after receipt by Tenant of notice in writing from Landlord specifying in reasonable detail the nature of such failure.

20.02 Tenant's Best Efforts.

In the event that the Default under Section 20.01(4) is of such a nature that it cannot be cured within such twenty (20) day period, then such Default shall not be deemed to be an Event of Default so long as Tenant, after receiving such notice, proceeds to cure the Default as soon as reasonably possible and continues to take all steps necessary to complete the same within a period of time which, under all prevailing circumstances, shall be reasonable. No such Default shall be deemed to be an Event of Default if and so long as Tenant shall be so proceeding to cure the same in good faith or be delayed in or prevented from curing the same by reason of Force Majeure.

ARTICLE 21
Insolvency

21.01 Insolvency.

If (1) there occurs with respect to Tenant an Insolvency or (2) any execution or attachment is issued against Tenant or any of its property and as a result thereof the Premises are taken or occupied by some Person other than the Tenant, except as may herein be permitted, then an Event of Default hereunder shall be deemed to have occurred so that the provisions of Article 22 hereof shall become effective and Landlord shall have the rights and remedies provided for therein.

ARTICLE 22
Landlord's Remedies; Damages on Default

22.01 Landlord's Remedies.

If an Event of Default shall occur and be continuing, Landlord may, at its option, give to Tenant a notice terminating this Lease upon a date specified in such notice, or Landlord may enter the Premises for the purpose of terminating this Lease, and upon the date specified in said notice or upon such entry the term and estate hereby vested in Tenant shall cease and any and all other right, title and interest of Tenant hereunder shall likewise cease without further notice or lapse of time, as fully and with like effect as if the entire Lease Term had lapsed, but Tenant shall continue to be liable to Landlord as hereinafter provided.

22.02 Surrender.

Upon any termination of this Lease as the result of an Event of Default, Tenant shall quit and peacefully surrender the Premises to Landlord. Upon or at any time after any such termination, Landlord may without further notice enter the Premises and possess itself thereof by summary proceedings or otherwise, and may dispossess Tenant and remove Tenant and all other Persons and property from the Premises and may have, hold and enjoy the Premises and the right to receive all rental income of and from the same.

22.03 Right to Relet.

At any time from time to time after any such termination, Landlord may relet the Premises or any part thereof, in the name of Landlord or otherwise, for such term or terms (which may be greater or less than the period which would otherwise have constituted the balance of the Lease Term) and on such conditions (which may include concessions or free rent) as Landlord, in its reasonable discretion, may determine and may collect and receive the rents therefor. Landlord shall in no way be responsible or liable for any failure to relet the Premises or any part thereof, or for any failure to collect any rent due upon any such reletting.

22.04 Survival of Covenants.

No such termination of this Lease shall relieve Tenant of its liability and obligations under this Lease and such liability and obligations shall survive any such termination. Tenant shall indemnify and hold Landlord harmless from all loss, cost, expense, damage or liability arising out of or in connection with such termination.

In the event of any such termination, Tenant shall pay to the Landlord the Rent up to the date of such termination. Tenant shall also pay to Landlord, on demand, as and for liquidated and agreed damages for Tenant's Default, the difference between

(1) the aggregate Rent which would have been payable under this Lease by Tenant from the date of such termination until the Stated Expiration Date, less

(2) the fair and reasonable rental value of the Premises for the same period, excluding Landlord's reasonable estimate of expenses to be incurred in connection with reletting the Premises, including, without limitation, all repossession costs, brokerage commissions, legal expenses, reasonable attorney's fees, alteration costs, and expenses of preparation for such reletting.

The amount derived from subtracting (2) from (1) above shall be discounted to present value at a rate of 6% per annum. If the Premises or any part thereof are relet by the Landlord before presentation of proof of such liquidated damages to any court, commission or tribunal, the amount of rent reserved upon such reletting shall be, prima facie, the fair and reasonable rental value for the part or the whole of the Premises so relet during the term of the reletting.

As additional and cumulative obligations after any such termination, Tenant shall also pay punctually to Landlord all the sums and shall perform all the obligations which Tenant covenants in this Lease to pay and to perform in the same manner and to the same extent and at the same time as if this Lease had not been terminated. In calculating the amounts to be paid by Tenant pursuant to the preceding sentence, Tenant shall be credited with any amount paid to Landlord pursuant to the second paragraph of this Section 22.04 and also with the net proceeds of any rent obtained by Landlord by reletting the Premises, after deducting all Landlord's reasonable expenses in connection with such reletting, including, without limitation, all repossession costs, brokerage commissions, fees for legal services and expenses of preparing the Premises for such reletting, it being agreed by Tenant that Landlord may (i) relet the Premises or any part or parts thereof for a term or terms which may at Landlord's option be equal to or less than or exceed the period which would otherwise have constituted the balance of the term hereof and may grant such concessions and free rent as Landlord in its reasonable judgement considers advisable or necessary to relet the same and (ii) make such alterations, repairs and decorations in the Premises as Landlord in its reasonable judgment considers advisable or necessary to relet the same, and no action of Landlord in accordance with the foregoing or failure to relet or to collect rent under reletting shall operate or be construed to release or reduce Tenant's liability as aforesaid.

Nothing herein contained shall limit or prejudice the right of the Landlord to prove for and obtain in proceedings for bankruptcy or insolvency by reason of the termination of this Lease, an amount equal to the maximum allowed by any statute or rule of law in effect at the time when, and governing the proceedings in which, such damages are to be proved, whether or not such amount be greater, equal to, or less than the amount of the difference referred to above. Notwithstanding the foregoing, in no event shall Tenant or Landlord be liable hereunder for any consequential, indirect or special damages or damages in the nature of list profits. Landlord shall make reasonable efforts to mitigate its damages hereunder.

22.05 Right to Equitable Relief.

If there shall occur a Default, Landlord shall be entitled to enjoin such Default and shall have the right to invoke any right and remedy allowed at law or in equity or by statute or otherwise as though re-entry, summary proceedings, and other remedies were not provided for in this Lease.

22.06 Right to Self Help; Interest on Overdue Rent.

If an Event of Default shall occur and be continuing, Landlord shall have the right upon reasonable notice to Tenant, but shall not be obligated, to enter upon the Premises and to perform the defaulted obligation notwithstanding the fact that no specific provision for such substituted performance by Landlord is made in this Lease with respect to such Event of Default. In performing such obligation, Landlord may make any payment of money or perform any other act. The aggregate of (i) all sums so paid by Landlord, (ii) interest (at the rate of 1 % per month or the highest rate permitted by law, whichever is less) on such sums and (iii) all necessary incidental

costs and expenses in connection with the performance of any such act by Landlord, shall be deemed to be Rent under this Lease and shall be payable to Landlord immediately upon demand. Landlord may exercise the foregoing rights without waiving any other of its rights or releasing Tenant from any of its obligations under this Lease.

All Rent not paid when due shall bear interest at the rate provided in the preceding paragraph, payable within 30 days after demand.

22.07 Payment of Landlord's Cost of Enforcement

Tenant shall pay, within 30 days after written demand, Landlord's reasonable expenses, including reasonable attorney's fees, incurred in enforcing any obligation of Tenant under this Lease or in curing any default by Tenant under this Lease as provided in Section 22.06.

22.08 Further Remedies.

Upon any termination of this Lease pursuant to Section 22.01, or at any time thereafter, Landlord may, in addition to and without prejudice to any other rights and remedies Landlord shall have at law or in equity, re-enter the Premises, and recover possession thereof and may dispossess any or all occupants of the Premises in the manner prescribed by the statute relating to summary proceedings, or similar statute(s); but Tenant in such case shall remain liable to Landlord as hereinbefore provided.

ARTICLE 23
Waivers

23.01 No Waivers.

Failure of Landlord or Tenant to complain of any act or omission on the part of the other party no matter how long the same may continue, shall not be deemed to be a waiver by said Landlord or Tenant of any of its rights hereunder. No waiver by either party of any provision of this Lease shall be deemed a waiver of a breach of the same or any other provision. No acceptance by Landlord of any partial payment shall constitute an accord or satisfaction but shall only be deemed a partial payment on account.

ARTICLE 24
Security Deposit

24.01 Security Deposit.

(a) Letter of Credit. As security for the full, faithful and timely performance of each of Tenant's obligations under the Lease, Tenant shall deliver to Landlord a Letter of Credit meeting the requirements contained in this Article 24, which issuance shall not be more than thirty (30) days after execution of this Lease.

(b) Amount of Letter of Credit. The amount of the Letter of Credit shall be Three Hundred Ninety-Five Thousand Two Hundred Sixty-Two and 90/100 Dollars ($395,262.90).

(c) Form of Letter of Credit. The Letter of Credit shall be irrevocable, unconditional and fully transferable one or more times without cost or expense to Landlord, shall be issued by Silicon Valley Bank or at another domestic bank reasonably acceptable to Landlord, and shall be in a form reasonably acceptable to Landlord. The Letter of Credit shall have an expiration date not less than one (1) year after the date of the Letter of Credit; and the beneficiary of the Letter of Credit shall be Landlord or Landlord's designee. The Letter of Credit shall also be self-extending with an outside expiration date not earlier than sixty (60) days following the Stated Expiration Date.

(d) Surrender of Security. As soon as reasonably practicable after the Lease Termination Date but not later than sixty (60) days following the expiration or termination of this Lease and the full satisfaction of all Tenant's obligations hereunder, Landlord shall return the Letter of Credit to Tenant.

(e) Letter of Credit as Security Deposit. If Tenant has deposited a Letter of Credit with Landlord, it will be treated as a security deposit (the "Security Deposit") pledged as security for the full, faithful and punctual performance by Tenant of all of the terms of this Lease. In the event Tenant defaults in the performance of any of the terms of this Lease beyond all applicable notice and cure periods, including, without limitation, the payment of Rent, or if Landlord is informed by the issuer of the Letter of Credit that the same will not be renewed and the Letter of Credit is not replaced by a substitute letter of credit at least twenty-one (21) days in advance of the Letter of Credit's scheduled expiration date, Landlord may use, apply or retain the whole or any part of the Security Deposit to the extent required for the payment of any Rent or for any sum which Landlord may expend or may be required to expend by reason of Tenant's default in respect of any of the terms of this Lease, including any damages or deficiency in the re-letting of the Premises, whether accruing before or after summary proceedings or other re-entry by Landlord. In the case of every such use, application or retention, Tenant shall, within ten (10) days after Landlord's request therefor, cause the amount of the Letter of Credit to be increased by the sum so used, applied or retained so that the Letter of Credit shall be replenished to its amount existing immediately prior thereto. The Security Deposit shall not be deemed a limitation on Landlord's damages or a payment of liquidated damages or a payment of the monthly Rent due for the last month of the Term of this Lease. If Tenant shall fully and punctually comply with all of the terms of this Lease, the Security Deposit, or so much of it as has not been applied by Landlord, shall be returned to Tenant after the termination of this Lease and after delivery of possession of the Premises to Landlord, within the time set forth above. In the event of a sale or lease of the building, Landlord shall have the right to transfer the Security Deposit to the vendee or lessee and upon such transfer and the vendee's or lessee's acknowledgement of receipt of the Security Deposit, Landlord shall immediately be released by Tenant from all liability for the return of such Security Deposit; and Tenant agrees to look solely to the new owner or landlord for the return of said Security Deposit; and it is agreed that the provisions hereof shall apply to every transfer or assignment made of the Security Deposit to a new owner or landlord. Tenant shall not assign or encumber or attempt to assign or encumber the Security Deposit and neither Landlord nor its successors or assigns shall be bound by any such assignment, encumbrance, attempted assignment or encumbrance. This Lease does not create a trust relationship between Landlord and Tenant with respect to such Security Deposit.

ARTICLE 25
General Provisions

25.01 Force Majeure.

In the event that Landlord or Tenant shall be delayed, hindered in or prevented from the performance of any act required hereunder by reason of Force Majeure, then performance of such act shall be excused for the period of the delay and the period for the performance of any such act shall be extended for a period equivalent to the period of such delay.

25.02 Notices and Communications.

All notices, demands, requests, consents, approvals and other communications provided for or permitted under this Lease shall be in writing, either delivered by hand or sent by registered or certified mail, postage prepaid or by a recognized courier which maintains delivery records, to the following address:

(a) if to Landlord at the address stated in Section 1.01 hereof, or at such other address as Landlord shall have designated in writing to the Tenant, with a copy to such Persons as Landlord shall have designated in writing to Tenant, or

(b) if to Tenant at the address stated in Section 1.01 hereof, or at such other address as the Tenant shall have designated in writing to the Landlord, with a copy to such Persons as Tenant shall have designated in writing to Landlord.

Any notice provided for herein shall become effective only upon and at the time of receipt by the Person to whom it is given, unless such notice is mailed by registered or certified mail, in which case it shall be deemed to be received on (i) the third Business Day following the mailing thereof or (ii) the day of its receipt, if a Business Day, or the next succeeding Business Day, whichever of (i) or (ii) shall be the earlier.

25.03 Tenant Estoppel Certificate.

Tenant shall, without charge, at any time and from time to time hereafter, within ten (10) Business Days after written request of Landlord, certify by written instrument duly executed and acknowledged to Landlord or any mortgagee or purchaser, or proposed mortgagee or proposed purchaser, or any Person specified in such request; (a) as to whether this Lease has been supplemented or amended, and if so, the substance and manner of such supplement or amendment, (b) as to the existence of any offsets, counterclaims or defenses thereto on the part of Tenant, (c) as to the existence of any Default or Event of Default, (d) as to the Term Commencement Date and Stated Expiration Date, and (e) as to any other matters as may reasonably be so requested, in the form of Exhibit F. Any such certificate may be relied upon by Landlord and any other Person to whom the same may be exhibited or delivered, and the contents of such certificate shall be binding on the party executing same.

Tenant shall in addition, within 5 Business Days after receipt from Landlord, execute and deliver to Landlord a tenant estoppel certificate substantially in the form attached hereto as Exhibit F.

25.04 Renewal.

If this Lease is renewed or extended the provisions of Section 7.01 shall not apply.

25.05 Governing Law.

This Lease and the performance thereof shall be governed, interpreted, construed and regulated by the laws of The Commonwealth of Massachusetts.

25.06 Partial Invalidity.

If any term, covenant, condition or provision of this Lease or the application thereof to any person or circumstance shall, at any time or to any extent, be invalid or unenforceable, the remainder of this Lease, or the application of such term or provision to persons or circumstances other than those as to which it is held invalid or unenforceable, shall not be affected thereby, and each term, covenant, condition and provision of this Lease shall be valid and be enforced to the fullest extent permitted by law.

25.07 Notice of Lease.

The parties will at any time, at the request of either one, promptly execute duplicate originals of an instrument, in recordable form, which will constitute a Notice of Lease, setting forth a description of the Premises and the Lease Term. The cost of review and recording shall be borne by Tenant.

25.08 Interpretation.

The Section headings used herein are for reference and convenience only and shall not enter into the interpretation hereof. This Lease may be executed in several counterparts, each of which shall be an original, but all of which shall constitute one and the same instrument.

25.09 Bind and Inure; Limitation of Landlord's Liability.

The obligations of this Lease shall run with the land, and this Lease shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns. No owner of the Land and Building shall be liable under this Lease except for breaches of Landlord's obligations occurring while owner of the Land and Building. The obligations of Landlord shall be binding upon the assets of Landlord which comprise the Land and Building but not upon other assets of Landlord. No individual partner, trustee, stockholder, officer, director, employee or beneficiary of Landlord shall be personally liable under this Lease and Tenant shall look solely to Landlord's interest in the Land and Building in pursuit of its remedies upon an event of default hereunder, and the general assets of Landlord and its partners, trustees, stockholders, officers, employees or beneficiaries of Landlord shall not be subject to levy, execution or other enforcement procedure for the satisfaction of the remedies of Tenant.

25.10 Parties.

Except as herein otherwise expressly provided, the covenants, conditions and agreements contained in this Lease shall be binding upon the heirs, successors and assigns of the Parties hereto.

25.11 Representations.

Landlord represents and warrants to Tenant that (a) the Building and the Premises are in material compliance with all Permitted Encumbrances and all applicable zoning, land use and environmental laws and agreements and the requirements of all easement and encumbrance documents and Landlord covenants to keep the same in compliance throughout the Term; (b) the uses of the Premises contemplated hereunder are permitted as of right at the Land; (c) Landlord holds fee simple title to the Land, subject to no mortgage; (d) Landlord has full power and authority to enter into this Lease and has obtained all consents and taken all actions necessary in connection therewith; and (e) no other party has any possessory right to the Premises or has claimed the same.

ARTICLE 26
Miscellaneous

26.01 HVAC.

HVAC hours for the office portion of the Premises shall be defined as from 8:00 AM to 6:00 PM Monday through Friday, excluding Holidays and 8:00 AM to 1:00 PM on Saturdays. HVAC hours for the lab portion of the Premises shall be controlled by Tenant with no restriction on hours of operation.

If Tenant shall require after-hours space heating or cooling for the office portion of the Premises, Landlord shall furnish such service at $55.00 per hour, subject to reasonable increases from time to time based upon electricity and equipment costs, provided that Tenant gives Landlord at least one (1) Business Day advance notice. In the event Tenant introduces onto the Premises equipment which overloads the systems, and/or in any other way causes the systems not adequately to perform their proper functions, supplementary systems may at Landlord's option be provided by Landlord at Tenant's expense.

Tenant shall have and operate its own dedicated HVAC system for the laboratory portion of the Premises that shall be separately metered and incur no after-hours charges.

Additional Air Conditioning Equipment

In the event Tenant requires additional air conditioning for business machines, meeting rooms or other special purposes, or because of occupancy or excess electrical loads, any additional air conditioning units, chillers, condensers, compressors, ducts, piping and other equipment, such additional air conditioning equipment will be installed, in such a manner that the same will not cause damage or injury to the Building or create a dangerous or hazardous condition. Such equipment will be installed by Tenant, subject to Landlord's prior approval of Tenant's plans and specifications for such work, which approval shall not be unreasonably withheld, delayed or conditioned. In such event: (i) such equipment shall be maintained, repaired and replaced by Tenant at Tenant's sole cost and expense, (ii) throughout the Term of this Lease, Tenant shall, at Tenant's sole cost and expense, purchase and maintain an appropriate service contract for such equipment from a service provider established in the field, and (iii) the location of such equipment shall not visually impact the Building or the operations of the Building.

26.02Holdover Clause.

In the event Tenant shall fail to vacate the Premises by the Lease Termination Date, Tenant shall pay Basic Rent to Landlord in an amount equal to 150% of the monthly Basic Rent. Tenant shall also pay all Additional Rent provided herein. The "Holdover Rental Rate" shall be paid monthly in advance to Landlord.

26.03Restoration.

At Landlord's election, Tenant shall, subject to the terms of this Lease, restore the Premises to its prior condition upon vacating the Premises.

26.04Brokerage.

Tenant warrants and represents to Landlord that it has had no dealings with any broker or agent in connection with this Lease other than Cushman & Wakefield and CBRE and covenants to defend, with counsel approved by Landlord, hold harmless and indemnify Landlord from and against any and all cost, expense or liability for any compensation, commissions and charges claimed by any broker or agent other than Cushman & Wakefield and CBRE. Landlord warrants and represents to Tenant that Landlord has had no dealings with any broker or agent in connection with this Lease other than Cushman & Wakefield and CBRE and covenants to defend, with counsel approved by Tenant, hold harmless and indemnify Tenant from and against any and all cost, expense or liability for any compensation, commissions and charges claimed by any broker or agent other than Cushman & Wakefield and CBRE. Landlord shall pay the commission payable to the brokers named in this section pursuant to separate agreement.

26.05 Landlord's Expenses Regarding Consents.

Tenant shall reimburse Landlord promptly on demand for all reasonable legal and other expenses incurred by Landlord in connection with all requests by Tenant for consent or approval hereunder in an amount not to exceed $5,000.

26.06 Signage.

Landlord, at Landlord's cost shall provide building standard tenant signage on the Building's park directory and lobby directory. Tenant, at Tenant's cost, shall be allowed to place its name on the entry to the Premises and on the façade of the Building. Tenant's sign on the Building façade shall be at the maximum size permitted by zoning (or by any zoning relief obtained by Tenant). The placement, installation, size and type of the Building sign shall be approved by Landlord which approval shall not be unreasonably withheld, delayed or conditioned and subject to all zoning and appeals by Governmental Authorities.

26.07Financial Statements.

Within ten (10) Business Days after request by Landlord from time to time but not more than one timer per calendar year, Tenant shall deliver to Landlord Tenant's audited financial statements (which shall be for the latest available year and in any event for a year ended not more than fifteen (15) months prior to Landlord's request), which, if Tenant is publicly held, may consist of Tenant's annual report to its shareholders. Such financial statements may be delivered to Landlord's mortgagees and lenders and prospective mortgagees, lenders, investors and purchasers.

26.08 Option to Extend.

Tenant shall have the option to extend the Term of this Lease for two (2) five (5) year extension term(s) ("Extension Term(s)") provided (i) no Event of Default shall exist at the time such option is exercised and (ii) Tenant shall give written notice to Landlord of its exercise of such option not less than twelve (12) months prior to expiration of the original term, **time being of the essence for the giving of such notice**. All of the terms and provisions of this Lease shall be applicable during the Extension Term except (a) Tenant shall have no option to extend the Lease Term beyond the Extension Term(s) and, (b) the Basic Rent for the Extension Term shall be at the then Market Rent but no less than the prior year's Basic Rent.

"Market Rent" shall be computed as of the applicable date at the then current rentals being charged to new tenants for comparable office space located in the vicinity of the Building, taking into account and giving effect to, in determining comparability, without limitation, such considerations as size, location, amenities and lease term.

Landlord shall initially designate the Market Rent. If Tenant disagrees with Landlord's designation of Market Rent, then Tenant shall have the right, by written notice given within twenty-one (21) days after Tenant has been notified of Landlord's designation, to submit such Market Rent to arbitration as follows. Market Rent shall be determined by arbitrators, one to be chosen by Tenant, one to be chosen by Landlord and a third to be selected, if necessary, as below provided. If within twenty (20) days after Tenant's notice, the parties agree upon a single arbitrator, Market Rent shall be determined by such arbitrator. The unanimous written decision of the two first chosen without selection and participation of a third arbitrator, or otherwise the written decision of a majority of the three arbitrators chosen and selected as provided herein, shall be conclusive and binding upon Landlord and Tenant. Landlord and Tenant shall each notify the other of its chosen arbitrator within twenty-one (21) days following the call for arbitration and, unless such two arbitrators shall have reached a unanimous decision within thirty (30) days after their designation, then they shall so notify the then President of the Greater Boston Real Estate Board and request that person to select an impartial third arbitrator, who shall be a real estate broker dealing with like types of properties, to determine Market Rent as herein defined. Such third arbitrator and the first two chosen shall hear the parties and their evidence and render their decision within thirty (30) days following the conclusion of such hearing and notify Landlord and Tenant thereof. Landlord and Tenant shall bear the expense of the third arbitrator (if any) equally. If the dispute between the parties as to Market Rent has not been resolved before the commencement of Tenant's obligation to pay rent under the Lease in Market Rent, then Tenant shall pay rent under the Lease in respect of the Premises based upon the Market Rent designated by Landlord until either the agreement of the parties as to the Market Rent or the decision of the arbitrators, as the case may be, at which time Tenant shall pay any underpayment of rent to Landlord, or Landlord shall refund any overpayment of rent to Tenant. Each arbitrator appointed under this section 26.08 must be independent and shall not have worked for either Landlord or Tenant within the five (5) immediate prior years.

26.09 Right of First Refusal

Provided this Lease is in full force and effect and has not otherwise expired or been terminated in accordance with the terms hereof, and further provided that Tenant is not then in default beyond any applicable notice and cure period provided for hereunder, Tenant shall have an ongoing right of first refusal (the "Right of First Refusal") to lease any available space in the Building which is offered by Landlord for lease to third party tenants after the date of this Lease and prior to the expiration or sooner termination of the Term of this Lease (as such term may be extended as provided herein) (the "Additional Space") in accordance with the provisions set forth below.

If Landlord receives a bona fide offer (the "Offer") from a third party to lease the Additional Space, and the Offer is acceptable to Landlord, Landlord shall, prior to acceptance of the Offer, provide Tenant with the terms of the Offer in writing (the "Offer Notice"). Tenant shall respond to Landlord in writing within twenty (20) business days after Tenant's receipt of the Offer Notice as to Tenant's decision either to lease the Additional Space or to waive its rights hereunder. Time is of the essence of this provision.

Tenant's failure to notify Landlord within such time shall be deemed an immediate waiver of Tenant's rights to lease such Additional Space. If Tenant timely notifies Landlord that it desires to lease the Additional Space covered by the Offer Notice, Landlord shall thereupon lease the Additional Space to Tenant (and Tenant shall accept such Additional Space) for the remainder of the Term of this Lease (as such term may be extended as provided herein) upon the same terms and conditions as contained in this Lease, except that the base rent payable for such Additional Space shall be equal to the then current Base Rent payable hereunder for the Premises (subject to future adjustments as set forth in this Lease with respect to the Premises) and Landlord shall provide Tenant an improvement allowance in an amount equal to a prorated portion of the Allowance (as hereinafter defined) based upon the then remaining initial term of this Lease.

If Tenant properly exercises its right to lease the Additional Space, the parties shall promptly thereafter execute an amendment to the Lease to include the Additional Space. If Tenant fails to timely and properly notify Landlord that Tenant desires to lease the Additional Space which is the subject of an Offer Notice, Landlord may lease such Additional Space to the third party identified in the Offer Notice and on the same terms as set forth in the Offer Notice. Thereafter, Landlord may not lease such Additional Space to a third party without first offering such Additional Space to Tenant in accordance with the terms of this Section.

Notwithstanding the foregoing, in no event shall Landlord be required to give Landlord's Offer Notice, and Tenant shall not have a Right of First Refusal, (a) prior to the Commencement Date or (b) if less than three (3) years will remain in the Term as of the date Landlord would deliver the Available Space to Tenant unless Tenant agrees to exercise an Extension Term.

26.10 Storage. Tenant shall have the right to install, maintain and use a Conex storage container in the parking lot, which storage container shall be in a location mutually acceptable to Tenant and Landlord as close as practicable to the rear of the Building. The size of the storage unit is anticipated to be equivalent to two (2) parking spaces and will generally be built in accordance with the plans attached hereto as Exhibit H.

ARTICLE 27
Entire Agreement

27.01 Entire Agreement.

No oral statement or prior written matter shall have any force or effect. This Agreement shall not be modified or canceled except by writing subscribed to by all parties.

No representations, inducement, promises or agreements, oral or otherwise, between Landlord and Tenant or any of their respective brokers, employees or agents, not embodied herein, shall be of any force or effect.

The submission of this Lease for examination, review, negotiation and/or signature shall not constitute an offer or an option to lease or a reservation of the Premises and is subject to withdrawal or modification at any time by either party. This Lease shall become effective and binding only if and when it shall be executed and delivered by both Landlord and Tenant.

Executed as a sealed instrument as of the 19th day of April, 2019.

LANDLORD:

Woburn MCB II, LLC

By: /s/ Janet A. Wallace
Janet A. Wallace
Its Vice President & Secretary

TENANT:

By:/s/ Thomas Kassberg
Printed Name: Thomas Kassberg
Title:Chief Business Officer

Exhibit 10.71

COMMERCIAL LEASE

This Commercial Lease **("Lease")** is made as of this 2nd day of July, 2018 (the "**Lease Date**") by and between **32 Leveroni LLC** ("**Landlord**") and **Ultragenyx Pharmaceutical, Inc.** ("**Tenant**").

BASIC LEASE INFORMATION

LANDLORD:	32 Leveroni LLC
TENANT:	Ultragenyx Pharmaceutical, Inc.
LANDLORD'S NOTICE ADDRESS:	32 Leveroni LLC 296 Olive Avenue Novato, CA 94945 Attention: Debi George with a copy to: 32 Leveroni LLC 49 Los Pinos Road Nicasio, CA 94946 Attention: Larry George
TENANT'S NOTICE ADDRESS:	Ultragenyx Pharmaceutical, Inc. 60 Leveroni Court Novato, CA 94949 Attention: Joseph J. Seiwert III with a copy to: Ultragenyx Legal Department Attention: General Counsel
PREMISES:	A 20,000 rentable square foot building located at 32 Leveroni Court, Novato, CA 94949, as identified in Exhibit A.
PERMITTED USE:	General office use and laboratory purposes and no other purpose.

OPTION TO PURCHASE	Tenant has an Option To Purchase the Premises subject to the terms and conditions as set forth in Section 18 of this Lease.
PARKING ALLOCATION:	(34) unreserved spaces at no additional charge and as identified in Exhibit A. Tenant shall be permitted to park Tenant's passenger vehicles, transfer trucks, trailers and tractors within designated areas ("Parking Area") as needed for the conduct of Tenant's business under the Lease.
ESTIMATED TERM COMMENCEMENT DATE:	Upon exercise of Tenant's Option To Lease and Landlord vacating Premises, which in no event shall exceed four (4) months from the date Tenant exercises the Option To Lease.
LEASE OF LEASE TERM:	Ten (10) years.
OPTION TO EXTEND LEASE	Tenant shall have the right to renew the Lease for two (2), five (5) year periods subject to the terms and conditions as set forth in Section 43 of this Lease.
BASE RENT	Months Per Square Foot Rental Rate Monthly Base Rent 1 – 12 $0.54 $10,800 13 – 24 $1.35 $27,000 As used herein, the term "**Lease Month**" means each full calendar month during the Lease Term (and if the Term Commencement Date does not occur on the first day of a calendar month, the first Lease Month shall begin on the first day of the first calendar month following the Term Commencement Date). Monthly Base Rent applicable for the period from the Term Commencement Date to the first day of the next calendar month shall be included with the payment of Base Rent and Operating Expenses in the first Lease Month for purposes of determining the monthly Base Rent rate applicable for such partial month.
LEASE RATE ESCALATOR:	There will be three percent (3%) annual escalations to the Base Rent starting on the twenty-fifth (25th) month and annually thereafter.
BASE RENT ABATEMENT:	Base Rent shall be partially abated for months 1-12 as identified above.
SECURITY DEPOSIT:	The equivalent of 1.5 months Base Rent and operating expenses, estimated to be $51,315.
TENANT'S PROPORTIONATE SHARE OF PREMISES:	100%

Expense	Estimate Per Sq. Ft.	Monthly Estimate**
Utilities:	$0.0227	$545.33
Common Area Maintenance:	$ 0.3160	$6,320.07
Insurance:	$.0251	$501.27
Management Fee:	$ .0113	$225.50
Estimated Total:	**$0.3751**	**$7,592.17**

ESTIMATED FIRST YEAR OPERATING COST:

LIABILITY INSURANCE LIMITS: $3,000,000 per occurrence; $5,000,000 annual aggregate.

LANDLORD'S WORK: Landlord, at Landlords sole choice, shall remove all warehouse racking systems and office furniture. Tenant shall have final approval, at Tenant's sole discretion, of all plans for the Tenant Improvements. (collectively, "**Landlord's Work**"):

BROKER: Kidder Mathews represented the Tenant in this transaction and the Landlord was self-represented.

The foregoing Basic Lease Information is incorporated into and made part of this Lease. Each reference in this Lease to any of the Basic Lease Information shall mean the respective information above and shall be construed to incorporate all of the terms provided under the particular section of the Lease pertaining to such information. In the event of any conflict between the Basic Lease Information and the Lease, the Basic Lease Information shall control.

[*REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK*]

By signing this Lease below, Landlord and Tenant agree to all the terms set forth in the Basic Lease Information above and all the General Lease Terms set forth in the provisions that follow on the succeeding pages, including all referenced Exhibits.

IN WITNESS WHEREOF, the parties have executed this Lease on the dates set forth below, to be effective as of the Lease Date set forth in the preamble paragraph above.

LANDLORD:

32 Leveroni LLC

By: /s/ Laurence George
Laurence George
Its:_____

By: /s/ Debra George
Debra George
Its:_____

Date of Execution: July 18, 2018

TENANT:

Ultragenyx Pharmaceutical, Inc.

By: /s/ Thomas Kassberg
Thomas Kassberg
Its: Chief Business Officer

By:_____
_____
Its:_____

Date of Execution: July 16, 2018

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GENERAL LEASE TERMS

1. PREMISES

Landlord and Tenant are parties to that certain Option To Lease Real Property Agreement, dated as of _____, 2018, (the "**Lease Option Agreement**"), pursuant to which Tenant has exercised its right to enter into this Lease ("**Option To Lease**"). Landlord leases to Tenant and Tenant leases from Landlord, upon the terms and conditions hereinabove and hereinafter set forth, those premises (the "**Premises**") outlined in red on Exhibit A and more fully described in the Basic Lease Information. The Premises are the entirety of the building described in the Basic Lease Information (outlined in blue on Exhibit A). The Premises are stipulated for all purposes of this Lease to contain the square footage set forth in the Basic Lease Information.

2. POSSESSION; LANDLORD'S WORK

The term commencement date (the "**Term Commencement Date**") shall be upon the exercise of Tenant's Option To Lease and Landlord's delivery of the Premises to Tenant in accordance with the Lease requirements. In no event shall the Term Commencement Date be later than four (4) months after the date Tenant exercises the Option To Lease (the "**Outside Commencement Date**"). Within ten (10) days after delivery of the Premises to Tenant, Tenant shall execute and deliver to Landlord a certificate in the form attached hereto as Exhibit D ("**Commencement Date Certificate**"). If for any reason Landlord cannot deliver possession of the Premises to Tenant by the Outside Commencement Date, and such delivery delay is not due to a delay caused solely by Tenant, Landlord shall be responsible for the full amount of any holdover fees or penalties incurred by Tenant, if any, as well as the liquidated damages discussed below, and Tenant shall not be obligated to pay Base Rent or perform any other obligation of Tenant under the terms of this Lease until Landlord delivers possession of the Premises to Tenant. If possession of the Premises is not delivered to Tenant within thirty (30) days after the Outside Commencement Date, Tenant may, at its option, by notice in writing to Landlord within ten (10) days after the end of said thirty (30) day period, cancel this Lease, in which event the parties shall be discharged from all obligations hereunder except that Landlord shall pay Tenant the full amount of any holdover fees or penalties incurred by Tenant as well as liquidated damages as set forth below. If Tenant is prevented from entering and using the Premises by the Outside Commencement Date for any reason except for a delay caused solely by Tenant, Landlord shall pay Tenant liquidated damages to address the harm suffered by Tenant as a result of the delay in the amount of five thousand dollars ($5000.00) ("**Liquidated Damages**") per calendar day of delay. Tenant shall not be liable for any Base Rent for any period prior to the Term Commencement Date. Landlord shall vacate the Premises no later than four (4) months after the date Tenant exercises the Option To Lease and shall deliver possession of the Premises to Tenant free and clear of any prior tenants or occupants, their trade fixtures and their personal property, unencumbered by any prior leases or tenancies, free of Hazardous Materials and in "broom clean" condition, with all building systems in good working order and condition, and with all utility and service connection charges paid. The parties recognize that as a material inducement to Tenant entering into this Lease, Landlord covenants and warrants, as of the Term Commencement Date, the following:

2.1 To the best of Landlord's knowledge, the Premises are structurally sound, free from material defects, and has been constructed in compliance with applicable local codes and regulations; the roof of the Premises is watertight and in good working order; and the water lines, gas mains, electric power lines, and sanitary and storm sewers located on the Premises are adequate for Tenant's intended use. The Premises (except those fixtures and equipment installed by Tenant) do conform or that Landlord will promptly cause them to conform to every applicable requirement of statutes, ordinances, rules, regulations and building codes in effect within the jurisdiction of the Premises, including, without limitation, the federal Americans with Disabilities Act ("**ADA**").

2.2 Landlord has no knowledge of, and Landlord has received no written notice of the pendency of, any litigation or proceeding pending, or to the best of Landlord's knowledge, threatened against Landlord relating to the Premises or any claim having been made by any governmental agency that a violation or violations of any applicable covenants or restrictions of record, applicable building codes, regulations, or ordinances exist with regard to the Premises as of the Term Commencement Date.

2.3 To the best of Landlord's knowledge, no Hazardous Material is present on, at, beneath, or below, migrating from or onto the Premises, which exceeds any cleanup objective set forth by a governmental authority having jurisdiction over the Premises or which could cause Tenant to incur liability under any Environmental Law and Landlord has not used any Hazardous Material at the Premises. The Premises does not contain any: (a) underground storage tank; (b) asbestos-containing material; (c) landfills or dumps; or (d) hazardous waste management facility as defined under the Resource Conservation and Recovery Act or any comparable state law; and to the best of Landlord's knowledge the Premises has not have at any time contained any of the items referenced in clauses (b), (c), or (d) of this section.

2.4 Without creating any independent duty or obligation on the part of Landlord to investigate, all matters materially and adversely impacting all or any part of the Premises, the ownership, operation, use or development of all or any part of the Premises, or with the potential of having such impact, which are known to Landlord have been disclosed to Tenant in writing. A material and/or adverse matter under this provision is understood by the parties to be a matter that would result in limiting or preventing the Tenant from utilizing the Premises as intended under this Lease.

2.5 If the Premises do not comply with the warranties in subsections (a)-(d) above, Landlord shall, except as otherwise provided in this Lease, promptly after receipt of written notice provided by Tenant at any time during the Lease Term and setting forth with specificity the nature and extent of such non-compliance, take such action, at Landlord's expense, as may be reasonable or appropriate to rectify the non-compliance and shall indemnify and hold Tenant harmless from any claim, damage or liability that may arise due to any such noncompliance with the warranties set forth herein.

3. TERM

3.1 **Length of Term**. The Term of this Lease shall commence on the Term Commencement Date and continue in full force and effect for the number of months specified as the Length of Term in the Basic Lease Information or until this Lease is terminated as otherwise

provided herein. If the Term Commencement Date is a date other than the first day of a calendar month, the Term shall be the number of months of the Length of Term in addition to the remainder of the calendar month following the Term Commencement Date.

4. USE

4.1 **General**. Tenant shall use the Premises for the Permitted Use set forth in the Basic Lease Information and for no other use or purpose. In all events, Tenant's use shall be in compliance with all applicable Regulations (as defined in Section 4(c) below). Tenant and Tenant's employees, agents, customers, visitors, invitees, licensees, contractors, assignees and subtenants (collectively, "**Tenant's Parties**") shall have the nonexclusive right to use, in common with other parties occupying the Premises, the Parking Areas, driveways and sidewalks of the Premises. In the event that Landlord has knowledge of dangerous conditions in and around the Premises, Landlord shall have the duty to protect the Tenant and the Premises from foreseeable criminal acts occurring in and around the Premises including providing security measures. Landlord shall be responsible for the costs of providing two (2) sets of keys to Tenant to access the Premises. Tenant shall be responsible for the cost of replacement keys during the Lease Term.

4.2 **Limitations**. Tenant shall not use or allow the Premises to be used for any improper, immoral, unlawful or objectionable purpose, nor shall Tenant cause or maintain or permit any nuisance in, on or about the Premises. Tenant shall not place any Hazardous Materials in the drainage system of the Premises except in compliance with Environmental Laws. No waste materials or refuse shall be dumped upon or permitted to remain outside the Premises except in trash containers placed inside exterior enclosures designed for that purpose by Landlord.

4.3 **Compliance with Regulations**. Subject to Landlord's warranty in Section 2 of this Lease and except for Environmental Conditions referenced in Exhibit B, by entering the Premises, Tenant accepts the Premises in the condition existing as of the date of such entry, subject to all existing municipal, state, federal and other governmental statutes, regulations, laws and ordinances applicable thereto, including (i) zoning ordinances, (ii) regulations governing and relating to the use, occupancy and possession of the Premises, including without limitation the Americans with Disabilities Act of 1990, (iii) regulations governing and relating to the use, storage, generation and disposal of Hazardous Materials (as defined in Section 31 below) in, on and under the Premises and (iv) any conditions, covenants and restrictions recorded against the Premises (all of the foregoing, including (i) through (iv) above, collectively, the "**Regulations**"). Except for Existing Environmental Conditions, Tenant shall, at Tenant's sole expense, strictly comply with all Regulations now in force or which may hereafter be in force relating to the Premises and the use of the Premises and/or the use, storage, generation of Hazardous Materials in, on and under the Premises. Tenant shall at its sole cost and expense obtain any and all licenses or permits necessary for Tenant's use of the Premises. Landlord shall be responsible for delivering the premises in ADA compliance at the Term Commencement Date.

5. RULES AND REGULATIONS

Tenant shall faithfully observe and comply with the rules and regulations set forth in Exhibit C, as well as any that Landlord may from time to time prescribe in writing for the purpose

of maintaining the proper care, cleanliness, safety, and general order of the Premises. Tenant shall cause Tenant's Parties to comply with such rules and regulations.

6. RENT

6.1 "**Rent**" shall mean Base Rent plus Additional Rent.

6.2 **Base Rent**. Tenant shall pay to Landlord, without notice or demand, throughout the Term, Base Rent as specified in the Basic Lease Information, payable in monthly installments in advance on or before the first day of each calendar month, in lawful money of the United States at the address specified in the Basic Lease Information or to such other place as Landlord may from time to time designate in writing.

6.3 **Additional Rent**. All monies other than Base Rent required to be paid by Tenant hereunder, including, but not limited to, the interest and late charge described in Paragraph 26, any monies spent by Landlord pursuant to Section 30, and Tenant's Proportionate Share of Basic Operating Cost, as specified in Section 7 below, shall be considered additional rent ("**Additional Rent**").

6.4 If the obligation for payment of Rent commences on other than the first day of a month, then Base Rent and Additional Rent shall be prorated and the prorated installment shall be paid on the first day of the calendar month next succeeding the Term Commencement Date.

7. BASIC OPERATING COST

7.1 **Basic Operating Cost**. In addition to the Base Rent required to be paid hereunder, Tenant shall pay throughout the Term as Additional Rent, Tenant's Proportionate Share, as set forth in the Basic Lease Information, of Basic Operating Cost for the Premises in the manner set forth below.

7.2 "**Basic Operating Cost**" shall mean all expenses and costs of every kind and nature which Landlord shall pay or become obligated to pay, because of or in connection with the management, maintenance, repair, preservation and operation of the Premises and its supporting facilities (determined in accordance with generally accepted accounting principles, consistently applied) including but not limited to the following:

(a) **Taxes**. All real property taxes, possessory interest taxes, business or license taxes or fees, service payments in lieu of such taxes or fees, annual or periodic license or use fees, excises, transit charges, housing fund assessments, open space charges, assessments, levies, fees or charges, general and special, ordinary and extraordinary, unforeseen as well as foreseen, of any kind (including fees in-lieu of any such tax or assessment) which are assessed, levied, charged, confirmed, or imposed by any public authority upon the Premises, its operations or the Rent (or any portion or component thereof) (all of the foregoing being hereinafter collectively referred to as "**real property taxes**"), or any tax imposed in substitution, partially or totally, or any tax previously included with the definition of real property taxes, or any additional tax the nature of which was previously included within the definition of real property taxes except (A) inheritance, estate or gift taxes imposed upon or assessed against the Premises, or any part

thereof or interest therein, and (B) taxes computed upon the basis of net income of Landlord or the owner of any interest therein, except as otherwise provided in the following sentence. Basic Operating Cost shall also include any taxes, assessments, or any other fees imposed by any public authority upon or measured by the monthly rental or other charges payable hereunder, including, without limitation, any gross income tax or excise tax levied by the local governmental authority in which the Premises is located, the federal government, or any other governmental body with respect to receipt of such rental, or upon, with respect to, or by reason of the development, possession, leasing, operation, management, maintenance, alteration, repair, use or occupancy by Tenant of the Premises or any portion thereof, or upon this transaction or any document to which Tenant is a party creating or transferring an interest or an estate in the Premises. In the event that it shall not be lawful for Tenant to reimburse Landlord for all or any part of such taxes, the monthly rental payable to Landlord under this Lease shall be revised to net to Landlord the same net rental after imposition of any such taxes on Landlord as would have been payable to Landlord prior to the payment of any such taxes.

(b) **Insurance**. All insurance premiums and costs, including but not limited to, any insurance deductible amounts incurred by Landlord, as more fully set forth in Section 8(a) below.

(c) **Repairs and Maintenance**. Repairs and general maintenance for the Premises shall be responsibility of Tenant during the Lease Term subject to Section 10 of this Lease.

(d) **Services**. All expenses relating to maintenance, janitorial, debris removal and service agreements and services, and costs of supplies and equipment used in maintaining the Premises and the equipment therein and the driveways, curbs, Parking Area, and service areas, including, without limitation, alarm service, window cleaning, elevator maintenance, and lighting fixture maintenance, landscaping shall be paid by Tenant, either directly or indirectly.

(e) **Utilities**. Utilities which benefit all or a portion of the Premises including without limitation electricity and water and sewer charges shall be paid by Tenant.

(f) **Legal and Accounting**. Legal and accounting expenses relating to the Premises, including the cost of audits by certified public accountants and tax consultants.

Basic Operating Cost shall not include the following: (1) costs, expenses, depreciation or amortization for capital improvements and capital repairs and capital replacements required to be made by Landlord under this Lease; (2) costs of restoration to the extent of net insurance proceeds received by Landlord with respect thereto; (3) replacement of or structural repairs to the roof or the exterior walls; (4) repairs to the extent covered by insurance proceeds, or paid by Tenant or other third parties; (5) alterations solely attributable to tenants of the Premises other than Tenant including but not limited to any costs associated with providing tenant improvements and renovations to any other tenants in the Premises; (6) marketing expenses; (7) the construction costs for any expansion of the Premises; (8) ground rent or debt service (including, but without limitation, interest and principal) required to be made on debt incurred by Landlord and relating to any portion of the Building or Project; (9) the cost of special services, goods or materials provided to any other tenant; (10) costs for which Landlord has a right to receive reimbursement from others;

(11) depreciation of the Premises or other said improvements; (12) costs occasioned by any fraud or willful misconduct by Landlord; (13) environmental pollution assessment and remediation related costs not caused by Tenant or its agents; (14) expenses paid from reserve amounts previously included in Operating Expenses; (15) costs of any items to the extent Landlord receives reimbursement from insurance proceeds or from a third party (such proceeds or reimbursement to be credited to Operating Expenses in the year in which received, except that any commercially reasonable deductible amount under any insurance policy shall be included within Operating Expenses charges when incurred by Landlord); (16) costs arising from Landlord's charitable or political contributions; (17) advertising and promotional expenditures, and the costs of acquiring and installing signs in or on the Premises selectively identifying any specific tenant of the Premises (as opposed to general Premises signage); (18) cost of the initial construction and installation of the Premises (including the Common Area) and of correcting any defects in or inadequacy of the initial design or construction of the Premises or of making any repairs of such initial construction to the extent covered by construction warranty; (19) tax penalties incurred or interest charged as a result of Landlord's failure to make payments for such items to the extent required by this Lease, except to the extent not caused by Tenant's failure to make such payments when due under this Lease; (20) attorneys' and other professional fees, costs and disbursements and other expenses incurred in connection with procuring new tenants and/or negotiations or disputes with present or prospective tenants or other occupants of the Premises, except to the extent incurred as a result of Tenant's acts or omissions; (21) repairs, alterations, additions, improvements or replacements made to rectify or correct any condition with respect to the Premises that is in violation of applicable laws on the date of execution of this Lease; (22) salaries, wages or other compensation paid to officers or executives of Landlord; (23) overhead and profit increment paid to a subsidiary, affiliate or other entity related to Landlord for services to the extent they are in excess of the amount that would be paid in the absence of such affiliation; (24) specific costs incurred for the account of, separately billed to and paid by specific tenants in the Premises; (25) any increase in real property taxes resulting from a change in ownership of the Premises that occurs during the Term of this Lease or any extensions or renewals thereof; and (26) income, excess profits, or franchise taxes or other such taxes imposed on or measured by the income of Landlord from the operation of the Premises.

7.3 **Payment of Estimated Basic Operating Cost.** "Estimated Basic Operating Cost" for any particular fiscal year shall mean Landlord's estimate of the Basic Operating Cost for such fiscal year made prior to commencement of such fiscal year as hereinafter provided. Landlord shall have the right from time to time to revise its fiscal year and interim accounting periods so long as the periods as so revised are reconciled with prior periods in accordance with generally accepted accounting principles consistently applied. During the last month of each fiscal year during the Term, or as soon thereafter as practicable, Landlord shall give Tenant written notice of the Estimated Basic Operating Cost for the ensuing fiscal year. Tenant shall pay Tenant's Proportionate Share of the Estimated Basic Operating Cost with installments of Base Rent for the fiscal year to which the Estimated Basic Operating Cost applies in monthly installments on the first day of each calendar month during such year, in advance. If at any time during the course of the fiscal year, Landlord determines that Basic Operating Cost is projected to vary from the then Estimated Basic Operating Cost by more than ten percent (10%), Landlord may, by written notice to Tenant and delivery of supporting documentation for such change, revise the Estimated Basic Operating Cost for the balance of such fiscal year, and Tenant's monthly

installments for the remainder of such year shall be adjusted so that by the end of such fiscal year Tenant has paid to Landlord Tenant's Proportionate Share of the revised Estimated Basic Operating cost for such year.

7.4 **Computation of Basic Operating Cost Adjustment**. "Basic Operating Cost Adjustment" shall mean the difference between Estimated Basic Operating Cost and Basic Operating Cost for any fiscal year determined as hereinafter provided. Within one hundred twenty (120) days after the end of each fiscal year or as soon thereafter as practicable, Landlord shall deliver to Tenant a statement of Basic Operating Cost for the fiscal year just ended, accompanied by a computation of the Basic Operating Cost Adjustment. If such statement shows that Tenant's payment based upon Estimated Basic Operating Cost is less than Tenant's Proportionate Share of Basic Operating Cost, then Tenant shall pay to Landlord the difference within twenty (20) days after receipt of such statement. If such statement shows that Tenant's payment of Estimated Basic Operating Cost exceeds Tenant's Proportionate Share of Basic Operating Cost, then (provided that Tenant is not in default under this Lease) Landlord shall at Landlord's option credit the difference to Tenant's Rent payment(s) next due hereunder or pay the difference to Tenant, in either case within twenty (20) days after delivery of such statement to Tenant. If this Lease has been terminated or the Term hereof has expired prior to the date of such statement, then the Basic Operating Cost Adjustment shall be paid by the appropriate party within twenty (20) days after the date of delivery of the statement. Should this Lease commence or terminate at any time other than the first day of a fiscal year, Tenant's Proportionate Share of Basic Operating Cost shall be prorated by reference to the exact number of calendar days during such fiscal year that this Lease is in effect. No delay by Landlord in submitting any statement shall constitute a waiver of Landlord's right to submit such statement or to collect Tenant's Proportionate Share of Basic Operating Cost due hereunder.

7.5 **Net Lease**. This shall be a net Lease and Base Rent shall be paid to Landlord absolutely net of all costs and expenses, except as specifically provided to the contrary in this Lease. The provisions for payment of Basic Operating Cost and the Basic Operating Cost Adjustment are intended to pass on to Tenant and reimburse Landlord for all costs and expenses of the nature described in Section 7(a) incurred in connection with the maintenance, repair, preservation and operation of the Premises.

7.6 **Tenant Audit**. Landlord must keep at its principal office separate, full, complete and proper books of account covering all costs and expenses of maintaining and operating the Premises and must preserve such books of account for at least two (2) years after the close of each calendar year, together with all vouchers, invoices, statements, payroll records and other documents evidencing the costs and expenses for that calendar year (collectively, the "**Expense Records**"). Landlord shall keep accurate records showing in detail all Basic Operating Cost provided for in this Lease. Tenant and its authorized agents (including accountants and attorneys) may, at any reasonable time, within this two (2) year period, inspect, copy and audit the Expense Records, at its expense during Landlord's normal business hours, subject to the following conditions: (1) Tenant shall deposit with Landlord the full amount in dispute; (2) there is no uncured event of default under this Lease; (3) the audit shall commence within fifteen (15) days after Landlord makes Landlord's books and records available to Tenant's auditor and shall conclude within thirty (30) days after commencement; and (4) Tenant and its accounting firm shall

treat any audit in a confidential manner and shall each execute Landlord's confidentiality agreement for Landlord's benefit prior to commencing the audit. Tenant shall deliver a copy of such audit to Landlord within five (5) business days of receipt by Tenant. This paragraph shall not be construed to limit, suspend or abate Tenant's obligation to pay Rent when due, including Tenant's Proportionate Share of Basic Operating Cost. After verification, Landlord shall credit any overpayment determined by the audit report against the next monthly payment(s) of Rent provided to be paid under this Lease, or, if no further Rent is due, refund such overpayment directly to Tenant within twenty (20) days of determination. Likewise, Tenant shall pay Landlord any underpayment determined by the audit report within twenty (20) days of determination. The foregoing obligations shall survive the expiration or earlier termination of this Lease. If Tenant does not give written notice of its election to audit during the referenced thirty (30)-day period, Landlord's Basic Operating Cost for the applicable fiscal year shall be deemed approved for all purposes, and Tenant shall have no further right to review or contest the same. If the audit proves that Landlord's calculation of Tenant's Proportionate Share of Basic Operating Cost for the fiscal year under inspection was overstated by more than ten percent (10%) in the aggregate, then, after verification, Landlord shall pay Tenant's actual reasonable out-of-pocket audit and inspection fees applicable to the review of said fiscal year statement within twenty (20) days after receipt of Tenant's invoice therefor.

7.7 **Tenant's Personal Property Taxes**. In addition to and wholly apart from Tenant's obligation to pay Tenant's Proportionate Share of Basic Operating Cost, Tenant shall be responsible for and shall pay prior to delinquency any taxes or governmental service fees, possessory interest taxes, fees or charges in lieu of any such taxes, capital levies, or other charges imposed upon, levied with respect to or assessed against Tenant's personal property. To the extent that any such taxes are not separately assessed or billed to Tenant, Tenant shall pay the amount thereof on demand once invoiced to Tenant by Landlord.

8. INSURANCE

8.1 **Landlord's Insurance**. At all times during the Term, Landlord shall procure and keep in full force and effect the following insurance:

(a) Special Risk property insurance insuring (i) the Premises, (ii) all improvements located therein, excluding Tenant's Property (as defined in Section 8(b)(i) below), (iii) Landlord's equipment located on the Premises, and (iv) common area furnishings, all in such amounts and with such deductibles as Landlord considers appropriate;

(b) Commercial general liability insurance insuring Landlord's interest in the Premises;

(c) Rental income insurance in an amount equal to one year's Base Rent; and

(d) Such other insurance as Landlord reasonably determines from time to time.

8.2 **Tenant's Insurance**. Tenant shall, at its sole cost and expense, procure and keep in full force and effect the following insurance:

(a) Special Risk property insurance on Tenant's Property for its full replacement value. Such policy shall contain an agreed amount endorsement in lieu of a co-insurance clause. "Tenant's Property" is herein defined to be personal property of Tenant and any improvements made by or for Tenant ;

(b) Commercial general liability insurance insuring Tenant against any liability arising out of its use, occupancy or maintenance of the Premises or the business operated by Tenant pursuant to the Lease. Such insurance shall provide a combined single limit for bodily injury and property damage in the amounts set forth in the Basic Lease Information. Such policy shall name Landlord, Landlord's wholly-owned subsidiaries, Landlord's property manager and any mortgagees of Landlord as additional insureds as their respective interests may appear;

(c) Workers' Compensation insurance as required by state law;

(d) If Tenant uses vehicles to carry out its business on or about the Premises, motor vehicles liability insurance with a combined single limit of not less than $1,000,000 for bodily injury and property damage; and

(e) Any other form or forms of insurance or increased amounts of insurance as Landlord or any mortgagees of Landlord may reasonably require from time to time.

All such policies shall be written in a form and with an insurance company licensed to do business in the State in which the Premises is located with a rating in Best's Insurance Guide of not less than "A:VII (satisfactory)" to Landlord and any mortgagees of Landlord, and shall provide that Landlord and any mortgagees of Landlord receive not less than thirty (30) days' prior written notice of any cancellation or reduction in coverage. Tenant's deductible amounts shall not exceed $1,000. Prior to or at the time that Tenant takes possession of the Premises, and as a condition thereof, Tenant shall deliver to Landlord copies of policies or certificates evidencing the existence of the required amounts and forms of coverage satisfactory to Landlord.

In addition, Tenant shall obtain certificates of insurance evidencing commercial general liability insurance, including completed operations, motor vehicle liability insurance and workers' compensation insurance in the amounts required above from any contractor or subcontractor engaged by Tenant for Alterations, repairs or maintenance at the Premises during the Term, and such liability insurance shall name the same parties as additional insureds as is described above, and shall provide that any loss shall be payable to Landlord and such other additional insured parties as their respective interests may appear.

8.3 **Forms of Policies**. All commercial general liability and special risk property policies maintained by Tenant shall be written as primary policies, not contributing with and not supplemental to the coverage that Landlord may carry.

8.4 **Waiver of Subrogation**. Notwithstanding anything to the contrary in this Lease, Landlord and Tenant, for themselves and their respective insurers, each agree to and do

hereby waive any and all claims, demands, actions and causes of action that each may have or claim to have against the other, and/or against any subsidiary or joint venture of such other party, for loss or damage to any property, whether real and personal, to the extent the same is caused by or results from risks (i) which are insurable under standard fire and extended coverage insurance or (ii) which are insured against under any policy of insurance covering the Premises or any portion thereof or property therein carried by the parties and in force at the time of such loss or damage, notwithstanding that any such loss or damage may be due to or result from the negligence of either party hereto or their respective employees or agents; provided, however, that this waiver shall not apply to the portion of any damage which is not reimbursed by the damaged party's insurance because of the deductible in the damaged party's insurance coverage.

8.5 **Adequacy of Coverage**. Landlord, its agents and employees make no representation that the limits of liability specified to be carried by Tenant pursuant to this Section 8 are adequate to protect Tenant and such minimum limits shall not relieve Tenant from any of its obligations under this Lease. If Tenant believes that any of such insurance coverage is inadequate, Tenant will obtain such additional insurance coverage, as Tenant deems adequate, at Tenant's sole expense.

8.6 **Certain Insurance Risks**. Tenant shall not do or permit to be done any act or thing upon the Premises or bring or keep anything therein which would (i) jeopardize or be in conflict with fire or other insurance policies covering the Premises or fixtures and property in the Premises; (ii) increase the rate of fire insurance applicable to the Premisesor cause a cancellation of said insurance; or (iii) subject Landlord to any liability or responsibility for injury to any person or persons or to property by reason of any business or operation being carried on upon the Premises.

9. INDEMNIFICATION, WAIVER AND RELEASE

9.1 **Tenant's Indemnification**. Except with respect to Existing Environmental Conditions or environmental contamination located below, above or related to the Premises and not caused by Tenant, and/or to the extent of any injury to persons or damage to property that is proximately caused by the gross negligence or willful misconduct of Landlord, its employees or agents, and subject to the provisions of Section 8(d) above, Tenant shall indemnify and hold the Landlord Indemnitees harmless from and against any and all demands, claims, causes of action, fines, penalties, damages, liabilities, judgments, and expenses (including, without limitation, reasonable attorneys' fees) incurred in connection with or arising from:

(a) The use or occupancy or manner of use or occupancy of the Premises by Tenant or any of the Tenant's Parties;

(b) Any activity, work, or thing done or permitted by Tenant in or about the Premises;

(c) Any breach by Tenant or by any of the Tenant's Parties of this Lease;

(d) Any injury or damage to the person, property or business of Tenant or any of the Tenant's Parties entering upon the Premises under the express or implied invitation of Tenant; and

(e) Any alleged violation by Tenant of any Regulation.

If any action or proceeding is brought against a Landlord Indemnitee by reason of any of the foregoing items (i) through (v), Tenant, upon written notice from such Landlord Indemnitee, shall defend the same at Tenant's expense, with counsel reasonably satisfactory to Landlord. Tenant's obligations pursuant to the foregoing indemnity shall survive the termination of this Lease.

9.2 **Landlord's Indemnification.** Except to the extent of any injury to persons or damage to property that is proximately caused by the gross negligence or willful misconduct of Tenant, its employees or agents, and subject to the provisions of Section 8(d) above, Landlord shall indemnify and hold Tenant, Tenant's agents, employees, directors, officers, shareholders, partners, contractors, and their respective successors and assigns (collectively, the "**Tenant Indemnitees**") harmless from and against any and all demands, claims, causes of action, fines, penalties, damages, liabilities, judgments, and expenses (including, without limitation, reasonable attorneys' fees) incurred in connection with or arising from Existing Environmental Conditions, environmental matters located below, above or related to Premises but not caused by Tenant, or Landlord's or Landlord's Parties' activities in, on or about the Premises, including, without limitation, Landlord's breach or default of any obligation of Landlord to be performed under the terms of this Lease, the conduct of Landlord's business, the nonobservance or nonperformance of any law, ordinance or regulation or the negligence or misconduct of Landlord or Landlord's Parties, the buildings and improvements located on the Premises arising out of repair, the leakage of Hazardous Materials, gas, oil, water, steam or electricity emanating from their usual conduits, or due to any cause whatsoever.

10. LANDLORD'S REPAIRS AND SERVICES

10.1 **Repairs and Services**. Landlord shall, at Landlord's expense and which shall not be passed through to Tenant as an item of Basic Operating Cost including those replacement items listed above, maintain the structural soundness of the structural beams of the roof, foundations and exterior walls of the Premises in good repair (including painting), reasonable wear and tear excepted. The term "**exterior walls**" as used herein shall not include windows, glass or plate glass, doors, special storefronts or office entries. Landlord shall perform on behalf of Tenant and other tenants of the Premises, as an item of Basic Operating Cost, the maintenance and repair of the Premises, and public areas of the Premises, including but not limited to pest extermination, the landscaped areas, Parking Areas, driveways, the truck staging areas, fire sprinkler systems, sanitary and storm sewer lines, utility services, electric and telephone equipment servicing the Premises' exterior lighting and anything which affects the operation and exterior appearance of the Premises, as determined by Landlord in its sole discretion and excluding any payments for services that Tenant may be making directly. In addition, Landlord shall, as an item of Basic Operating Cost, enter into a regularly scheduled preventive maintenance/service contract with a licensed maintenance contractor selected by Tenant for servicing all hot water, heating,

ventilation and air conditioning ("**HVAC**") systems and associated equipment within or serving the Premises, which HVAC maintenance/service contract will include all services suggested by the equipment manufacturer within the operation/maintenance manual. Except for the expenses directly involving the items specifically described in the first sentence of this Section 10, Tenant shall reimburse Landlord for all such costs in accordance with the terms of Section 7. Any damage caused by or repairs necessitated by any act of Tenant may be repaired by Landlord at Landlord's option and at Tenant's expense. Tenant shall immediately give Landlord written notice of any defect or need for repairs after which Landlord shall commence repair of same within ten (10) business days of receipt of such notice. Landlord and Landlord's agent's liability with respect to any defects, repairs, or maintenance for which Landlord is responsible under any of the provisions of this Lease shall be limited to the cost of such repairs or maintenance unless caused by Landlord's negligence. Landlord warrants and represents that the HVAC systems for the Premises are in good working order as of the date hereof and will remain so for the initial twelve (12) months of the term of this Lease, ordinary wear and tear and negligence of Tenant excepted; in the event that any such systems and/or equipment fail during said twelve-month period, the cost to repair or replace shall be the sole responsibility of Landlord and no portion of such cost will be passed through to Tenant.

10.2 **Exemption of Landlord from Liability**. Landlord shall not be liable for any damage or injury to the person, business (or any loss of income therefrom), goods, wares, merchandise or other property of Tenant or any of Tenant's Parties or any other person in or about the Premises, whether such damage or injury is caused by or results from (i) fire, steam, electricity, water, gas or rain; (ii) the breakage, leakage, obstruction or other defects of pipes, sprinklers, wires, appliances, plumbing, air conditioning or lighting fixtures or any other cause; (iii) conditions arising in or about the Premises; or (iv) theft, riot, strike, injunction, war, terrorist act or act of God. The provisions of this Section 10(b) shall not, however, exempt Landlord from liability for Landlord's gross negligence or willful misconduct or for Existing Environmental Conditions and environmental matters located below, above or related to Premises but not caused by Tenant.

11. TENANT'S REPAIRS

11.1 **Maintenance and Repairs**. Tenant shall at Tenant's expense maintain all parts of the Premises in a good, clean, secure and fully-operative condition and promptly make all necessary repairs, including but not limited to, all windows, glass, interior doors, interior walls and wall finishes, floor covering, ceilings, truck doors, dock bumpers, dock plates and levelers, plumbing work and fixtures, downspouts, electrical and lighting systems (bulbs and ballasts), freight elevator, and fire sprinklers. Tenant shall at Tenant's expense also perform regular removal of trash and debris from the Premises. Tenant shall not damage any demising wall or disturb the integrity and support provided by any demising wall and shall, at its sole expense, immediately repair any damage to any demising wall caused by Tenant or any of Tenant's Parties.

11.2 **Exemption of Tenant from Liability.** Tenant shall not be liable for any damage or injury to the person, business (or any loss of income therefrom), goods, wares, merchandise or other property of Tenant or any of Tenant's Parties or any other person in or about the Premises, whether such damage or injury is caused by or results from (i) fire, steam, electricity, water, gas or rain; (ii) the breakage, leakage, obstruction or other defects of pipes, sprinklers, wires,

appliances, plumbing, air conditioning or lighting fixtures or any other cause; (iii) conditions arising in or about the Premises or upon other portions of the Premises, or from other sources or places; (iv) theft, riot, strike, injunction, war, terrorist act or act of God; or (v) any act or omission of any other tenant of the Premises. The provisions of this Section 11(b) shall not, however, exempt Tenant from liability for Tenant's gross negligence or willful misconduct.

12. ALTERATIONS

Tenant shall be responsible for the design and construction of the tenant improvements ("**Tenant Improvements**" or "**Alterations**"). Tenant shall have final approval, at Tenant's sole discretion, of all plans for the Tenant Improvements in, about or to the Premises without obtaining the prior written consent of Landlord. However, Tenant shall provide Landlord with written notice outlining the proposed Tenant Improvements. Tenant shall have the right to select the general contractor and/or subcontractors for any Alterations, subject to Landlord's approval which shall not be unreasonably withheld. Landlord shall not charge any construction management fee. With respect to any Alterations, Tenant shall: (a) comply with all applicable Regulations; and (b) will not interfere with the use and occupancy of any other portion of the Premises by any other tenant or its invitees. All Alterations made by Tenant shall remain the property of Tenant until termination of this Lease, at which time they shall be and become the property of Landlord if Landlord so elects; provided, however, that Landlord may, at Landlord's option, require that Tenant, at Tenant's expense, remove any or all Alterations made by Tenant and restore the Premises to their prior condition by the termination of this Lease provided that Tenant shall be notified in writing of any such requirement at the time Landlord provide consent to the Alterations. Notwithstanding the foregoing, Tenant shall remove from the Premises any specialized Tenant Improvements that were paid for or installed for Tenant's use during the Lease Term. All removals and restoration shall be accomplished in a good and workmanlike manner so as not to cause any damage to the Premises whatsoever and in compliance with Section 33 of this Lease. Tenant shall not be responsible for the removal or restoration costs associated with any Tenant Improvements that were completed prior to the Term Commencement Date.

13. LIENS

Tenant shall keep the Premises free from liens arising out of or related to work performed, materials or supplies furnished, or obligations incurred by Tenant in connection with any Alterations or other work made, suffered or done by or on behalf of Tenant in or on the Premises. In the event that Tenant shall not, within ten (10) days following the imposition of any such lien, cause the same to be released of record by payment or posting of a proper bond, Landlord shall have, in addition to all other remedies provided herein and by law, the right, but not the obligation, to cause the same to be released by such means as Landlord shall deem proper, including payment of the claim giving rise to such lien. All sums paid by Landlord on behalf of Tenant and all expenses incurred by Landlord in connection therewith shall be payable to Landlord by Tenant on demand with interest at the prevailing interest rate from the date of payment by Landlord. Landlord shall have the right at all times to post and keep posted on the Premises any notices permitted or required by law, or which Landlord shall deem proper, for the protection of Landlord, the Premises, and any other party having an interest therein, from mechanics' and materialmen's liens, and Tenant shall give Landlord not less than ten (10) business days' prior written notice of the

commencement of any work in the Premises which could lawfully give rise to a claim for mechanics' or materialmen's liens.

14. SIGNS

Tenant shall be permitted to install, at Tenant's sole cost, identity signage above the storefront of the Premises and a panel on the existing monument signage, if available, subject to Landlord's signage criteria, if any, and applicable Regulations. Any such signage shall be maintained by Tenant throughout the Term. Tenant shall remove all such signs and graphics prior to the termination of this Lease.

15. LANDLORD'S ACCESS

15.1 **Landlord's Access to Premises**. After seventy-two (72) hours written notice, except in emergencies that threaten life or property where no such notice shall be required, Landlord, and Landlord's agents and representatives, shall have the right to enter the Premises to inspect the same, to clean, to perform such work as may be permitted or required hereunder, to make repairs or alterations to the Premises or to other tenant spaces therein, to deal with emergencies, to post such notices as may be permitted or required by law to prevent the perfection of liens against Landlord's interest in the Premises, to exhibit the Premises to prospective tenants, purchasers, lenders or others, or for any other purpose as Landlord may deem necessary or desirable; provided, however, that Landlord shall use commercially reasonable efforts not to unreasonably interfere with Tenant's business operations. Tenant shall not be entitled to any abatement of Rent by reason of the exercise of any such right of entry. At any time within six (6) months prior to the end of the Term, Landlord shall have the right to erect on the Premises a suitable sign indicating that the Premises are available for lease.

16. UTILITIES

Tenant shall pay directly to the appropriate supplier for all gas, heat, air conditioning, light, power, telephone, trash, telecommunications and other utilities and services used on or from the Premises, together with any taxes, penalties, surcharges or the like pertaining thereto, and maintenance charges for utilities, and shall furnish all electric light bulbs, ballasts and tubes. If any such services are not separately metered to Tenant, Tenant shall pay a reasonable proportion of all charges jointly serving other premises. Landlord shall not be liable for any damages directly or indirectly resulting from nor shall the Rent or any monies owed Landlord under this Lease herein reserved be abated by reason of: (a) the installation, use or interruption of use of any equipment used in connection with the furnishing of any such utilities or services; (b) the failure to furnish or delay in furnishing any such utilities or services when such failure or delay is caused by acts of God or the elements, labor disturbances of any character, or any other accidents or other conditions beyond the reasonable control of Landlord; or (c) the limitation, curtailment, rationing or restriction on use of water, electricity, gas or any other form of energy or any other service or utility whatsoever serving the Premises; unless any such interruption results from the negligence or intentional misconduct of Landlord or its agents, employees or contractors. If any utility service to the Premises is interrupted as a result of the negligence or intentional misconduct of Landlord or its agents, employees or contractors and such interruption continues for seven (7) consecutive calendar days, Base Rent shall be equitably abated until such service is fully restored and such

abatement shall be Tenant's sole remedy. Landlord shall be entitled to cooperate voluntarily and in a reasonable manner with the efforts of national, state or local governmental agencies or utility suppliers in reducing energy or other resource consumption. The obligation to make services available hereunder shall be subject to the limitations of any such voluntary, reasonable program. Tenant shall provide its own janitorial services for the Premises.

17. SUBORDINATION

Without the necessity of any additional document being executed by Tenant for the purpose of effecting a subordination, this Lease shall be subject and subordinate at all times to: (a) all ground leases or underlying leases which may now exist affecting the Premises and a correct copy thereof shall have been provided to Tenant prior to the execution of this Lease, and (b) any mortgage or deed of trust which may now exist or hereafter be placed upon the Premises, any advances made on the security thereof and any renewals, modifications, consolidations, replacements or extensions thereof, whenever made or recorded. Notwithstanding the foregoing, Landlord shall have the right to subordinate or cause to be subordinated any such ground leases or underlying leases or any such mortgages or deeds of trust to this Lease on notice to Tenant. In the event that any ground lease or underlying lease terminates for any reason or any mortgage or deed of trust is foreclosed or a conveyance in lieu of foreclosure is made for any reason, Tenant shall, notwithstanding any subordination, attorn to and become the Tenant of the successor-in-interest to Landlord at the option of such successor-in-interest, provided that Tenant shall have no claim against such successor-in-interest arising from Landlord's acts or omissions occurring prior to such termination, foreclosure or conveyance in lieu thereof. Within ten (10) business days after request by Landlord, Tenant shall execute and deliver any additional documents evidencing Tenant's attornment or the subordination of this Lease with respect to any such ground leases or underlying leases or any such mortgage or deed of trust, in the form requested by Landlord or by any ground lessor, mortgagee, or beneficiary under a deed of trust; however, failure of Tenant to timely provide such documents shall not be an event of default.

18. OPTION TO PURCHASE

18.1 **Grant of Option To Purchase.** Landlord hereby grants to Tenant and Tenant hereby acquires from Landlord an option to purchase ("Option to Purchase") the Premises on the terms and conditions set forth in this Lease.

18.2 **Term of Option To Purchase.** The term of the Option To Purchase shall commence on the thirty-sixth (36th) month of the Lease Term and expire at 5:00 p.m. (PST) on expiration of the Lease, unless terminated earlier as provided herein ("**Option To Purchase Term**").

18.3 **Exercise of Option To Purchase.** So long as Tenant in not in material default under the Lease, Tenant may exercise the Option To Purchase, if at all, after the thirty-sixth (36th) month of the Lease Term and Tenant and/or any entity controlling Tenant, controlled by Tenant or under common control with Tenant (a "**Tenant Affiliate**") shall have an ongoing right to purchase the Premises through the end of the Lease Term ("**Exercise Period**"), by delivering to Landlord a written notice stating that Tenant has elected to exercise the Option To Purchase and will purchase the Premises on the terms and conditions set forth in this Lease. The applicable

written notice given pursuant to this Section 18 (c) is hereinafter referred to as the "**Option To Purchase Notice**."

18.4 **Purchase Price and Terms.** If the Option To Purchase is exercised during the fourth (4th) year of the Lease Term, the purchase price for the Premises shall be FIVE MILLION FIVE HUNDRED THOUSAND DOLLARS ($5,500,000.00) (the "**Purchase Price**"). If the Option To Purchase is exercised during or after the fifth (5th) year of the Lease Term, the Purchase Price shall increase annually by three percent (3%). The parties shall open an escrow with First American Title Company ("**Escrow Holder**") within five (5) days of delivery of the Option To Purchase Notice. The escrow for the sale of the Premises shall close no later than ninety (90) days following the opening of escrow. The parties shall execute standard escrow instructions prepared by Escrow Holder. All title insurance, escrow, recording, transfer and other costs of sale shall be paid by the party as is customary in the county where the Premises are located.

18.5 **Termination of Option To Purchase.** If Tenant does not exercise the Option To Purchase timely and properly during the Exercise Period as set forth in Section 18 (c) above, the Option To Purchase shall automatically terminate without further need of any documentation.

18.6 **Purchase and Sale.** Upon the timely and proper exercise of the Option To Purchase by Tenant, Landlord hereby agrees to sell the Premises to Tenant and Tenant hereby agrees to purchase the Premises from Landlord upon and subject to the terms and conditions set forth in this Lease.

18.7 **Memorandum of Option To Purchase.** Following the execution of this Lease, Landlord shall promptly record a memorandum (the "**Memorandum**") of this Option To Purchase in a form reasonably acceptable to Tenant which shall be recorded in the official records of the county recorder at Tenant's cost.

19. ESTOPPEL CERTIFICATE

Tenant agrees from time to time, within ten (10) business days after written request of Landlord, to execute and deliver to Landlord, or Landlord's designee, an estoppel certificate stating that this Lease is in full force and effect and has not been modified (or stating any such modifications), the date to which Rent has been paid, the expiration date of this Lease, that Landlord is not in default under this Lease (or specifying any claimed defaults), and such other matters pertaining to this Lease as may be reasonably requested by Landlord. Failure by Tenant to execute and deliver such certificate shall not be an event of default but shall constitute an acceptance of the Premises and acknowledgment by Tenant that the statements included are true and correct without exception. Landlord and Tenant intend that any statement delivered pursuant to this Section 19 may be relied upon by any mortgagee, beneficiary, purchaser or prospective purchaser of the Premises or any interest therein.

20. SECURITY DEPOSIT

Upon execution of this Lease, Tenant shall deposit with Landlord an amount equivalent to 1.5 months' Rent, which is estimated to be FIFTY-ONE THOUSAND THREE HUNDRED AND FIFTEEN DOLLARS ($51,315.00).

21. ASSIGNMENT AND SUBLETTING

21.1 **General**. Tenant shall not assign or sublet the Premises or any part thereof without Landlord's prior written approval, which approval shall not be unreasonably withheld. If Tenant desires to assign this Lease or sublet any or all of the Premises, Tenant shall give Landlord written notice at least thirty (30) days prior to the anticipated effective date of the assignment or sublease. Failure by Landlord to approve a proposed assignee or subtenant shall not cause a termination of this Lease.

21.2 **Rental Profits**. In the event of an assignment of sublet, after recovery of Tenant's brokerage fees, subleasing expenses, and unamortized Tenant Improvements, Tenant shall retain fifty percent (50%) of any rental profits.

21.3 **Tenant Affiliate**. Notwithstanding the above, Tenant may assign or sublet the Premises, or any part thereof, to any entity controlling Tenant, controlled by Tenant or under common control with Tenant (a "**Tenant Affiliate**"), with the prior written consent of Landlord.

22. CONDEMNATION

22.1 **Condemnation Resulting in Termination**. If the whole or any substantial part of the Premises should be taken or condemned for any public use under governmental law, ordinance or regulation, or by right of eminent domain, or by private purchase in lieu thereof, and the taking would prevent or materially interfere with the Permitted Use of the Premises, this Lease shall terminate and the Rent shall be abated during the unexpired portion of this Lease, effective when the physical taking of said Premises shall have occurred.

22.2 **Condemnation Not Resulting in Termination**. If a portion of the Premises should be taken or condemned for any public use under any governmental law, ordinance, or regulation, or by right of eminent domain, or by private purchase in lieu thereof, and this Lease is not terminated as provided in Section 22(a) above, this Lease shall continue in full force and effect, provided that within 60 days (i) Landlord shall proceed with reasonable diligence to restore the remainder of the Premises to the extent feasible and to ensure that the Premises or remainder thereof is restored to a tenantable condition and (ii) the Rent payable hereunder during the unexpired portion of the Lease shall be reduced, beginning on the date when the physical taking shall have occurred, to such amount as may be fair and reasonable under all of the circumstances.

22.3 **Award**. Landlord shall be entitled to any and all payment, income, Rent, award, or any interest therein whatsoever which may be paid or made in connection with such taking or conveyance and Tenant shall have no claim against Landlord or otherwise for the value of any unexpired portion of this Lease. Notwithstanding the foregoing, any compensation

specifically awarded Tenant for loss of business, Tenant's personal property, moving costs or loss of goodwill, shall be and remain the property of Tenant.

23. CASUALTY DAMAGE

23.1 **Casualty; Notice to Tenant**. If the Premises are damaged by fire or other insured casualty (each, a "**Casualty**"), Tenant shall immediately notify Landlord. Within thirty (30) days following the Casualty, Landlord shall give Tenant written notice of the time which will be needed to repair such damage, as determined by Landlord in its reasonable discretion, and the election (if any) which Landlord has made according to this Section 23. The date of delivery of Landlord's notice will be the "**Notice Date**" for purposes of this Section 23.

23.2 **Repair Period**. If the Premises are damaged by Casualty to an extent which may be repaired within one hundred twenty (120) days after the Notice Date, as reasonably determined by Landlord, Landlord shall promptly begin to repair the damage after the Notice Date, to the extent set forth in Section 23(f) below, and Landlord will diligently pursue the completion of such repair. In that event, this Lease will continue in full force and effect except that Rent shall be abated on a pro rata basis from the date of the Casualty until the date of the completion of such repairs (the "**Repair Period**") based on the proportion of the rentable area of the Premises Tenant is unable to use during the Repair Period.

23.3 **Options in Event of Major Damage**. If the Premises are damaged by Casualty to an extent that they may not be repaired within one hundred twenty (120) days after the Notice Date, as reasonably determined by Landlord, then (1) Landlord may cancel this Lease as of the date of such Casualty by written notice given to Tenant on or before the sixtieth (60th) day following the Casualty or (2) Tenant may cancel this Lease as of the date of such Casualty by written notice given to Landlord within ten (10) days after Landlord's delivery of its written notice that the repairs cannot be made within such one hundred twenty (120)-day period. If neither Landlord nor Tenant so elects to cancel this Lease, Landlord shall diligently proceed to repair the Premises, to the extent set forth in Section 23(f) below, and Rent shall be abated on a pro rata basis during the Repair Period based on the proportion of the rentable area of the Premises Tenant is unable to use during the Repair Period.

23.4 **Landlord's Termination Rights**. Notwithstanding the provisions of Sections 23(a), (b) and (c), above, if the Premises are damaged by an uninsured casualty, or if the proceeds of insurance are insufficient to pay for the repair of any damage to the Premises, or if the Casualty occurs during the last six (6) months of the Term, Landlord shall have the option to repair such damage or cancel this Lease as of the date of the damage by written notice to Tenant given on or before the sixtieth (60th) day following the occurrence of the damage.

23.5 **Tenant's Obligations**. If any Casualty is the result of the willful conduct or negligence or failure to act of Tenant, its agents, contractors, employees, or invitees, there will be no abatement of Rent as otherwise provided for in this Section 23.

23.6 **Landlord's Obligation to Repair**. Notwithstanding anything contained herein to the contrary, Landlord's obligations for repair of damage to the Premises shall include Tenant's Property and Tenant's Alterations. Landlord shall be responsible for the repair,

replacement and restoration of Tenant's Property and Alterations and shall promptly commence such repair and diligently pursue the same to completion unless this Lease is terminated as provided in this Section 23.

24. HOLDING OVER

Tenant shall vacate the Premises upon the expiration or sooner termination of this Lease. If Tenant shall retain possession of the Premises or any portion thereof without Landlord's consent following the expiration or sooner termination of the Lease for any reason, then Tenant shall pay to Landlord for each day of such retention one hundred twenty-five percent (125%) for up to three (3) months after the expiration or sooner termination of the Lease.

25. DEFAULT

25.1 **Events of Default**. The occurrence of any of the following shall constitute an event of default on the part of Tenant:

(a) **Nonpayment of Rent**. Failure to pay any installment of Rent or any other amount due and payable hereunder upon the date when said payment is due. Failure to pay Rent shall be subject to a cure period of ten (10) business days after Tenant's receipt of written notice from Landlord to Tenant.

(b) **Mechanics' Lien**. Without limiting Tenant's obligation to comply fully with the Required Mechanics Lien Protections in each applicable instance, failure to release of record any mechanics' lien filed against the Premises or the Premises within twenty (20) days following imposition of such lien.

(c) **Other Obligations**. Failure to perform any obligation, agreement or covenant under this Lease other than those matters specified in clauses (i), (ii) and (iii) of this Section 25(a), such failure continuing for thirty (30) days after written notice of such failure; provided, however, that if more than thirty (30) days are reasonably required to complete such performance, Tenant shall not be in default if Tenant commences such performance within the thirty (30)-day period and thereafter diligently pursues its completion. The notice required by this clause (iv) is intended to satisfy any and all notice requirements imposed by law on Landlord and is not in addition to any such requirement.

(d) **General Assignment**. A general assignment by Tenant for the benefit of creditors.

(e) **Bankruptcy**. The filing of any voluntary petition in bankruptcy by Tenant, or the filing of an involuntary petition by Tenant's creditors, which involuntary petition remains undischarged for a period of thirty (30) days. In the event that under applicable law the trustee in bankruptcy or Tenant has the right to affirm this Lease and continue to perform the obligations of Tenant hereunder, such trustee or Tenant shall, in such time period as may be permitted by the bankruptcy court having jurisdiction, cure all defaults of Tenant hereunder outstanding as of the date of the affirmance of this Lease and provide to Landlord such adequate

assurances as may be necessary to ensure Landlord of the continued performance of Tenant's obligations under this Lease.

(f) **Receivership**. The employment of a receiver to take possession of substantially all of Tenant's assets or the Premises, if such appointment remains undismissed or undischarged for a period of ten (10) days after the order therefor.

25.2 **Attachment**. The attachment, execution or other judicial seizure of all or substantially all of Tenant's assets or the Premises, if such attachment or other seizure remains undismissed or undischarged for a period of ten (10) days after the levy thereof.

25.3 **Remedies Upon Default**.

25.4 **Termination**. In the event of the occurrence of any event of default, subject to applicable cure periods, Landlord shall have the right to give a written termination notice to Tenant, and on the date specified in such notice, Tenant's right to possession shall terminate, and this Lease shall terminate unless on or before such date all arrears of rental and all other sums payable by Tenant under this Lease and all costs and expenses incurred by or on behalf of Landlord hereunder shall have been paid by Tenant and all other events of default of this Lease by Tenant at the time existing shall have been fully remedied to the satisfaction of Landlord. At any time after such termination, Landlord may recover possession of the Premises or any part thereof and expel and remove therefrom Tenant and any other person occupying the same, by any lawful means, and again repossess and enjoy the Premises without prejudice to any of the remedies that Landlord may have under this Lease, or at law or equity, by reason of Tenant's default or of such termination.

25.5 **Continuation After Default**. Even though an event of default may have occurred, this Lease shall continue in effect for so long as Landlord does not terminate Tenant's right to possession under Section 25(b)(i) above, and Landlord may enforce all of Landlord's rights and remedies under this Lease, including without limitation, the right to recover Rent as it becomes due, and Landlord, without terminating this Lease, may exercise all of the rights and remedies of a landlord. Acts of maintenance, preservation or efforts to lease the Premises or the appointment of a receiver upon application of Landlord to protect Landlord's interest under this Lease shall not constitute an election to terminate Tenant's right to possession.

25.6 **Other Remedies**. In the event of the occurrence of any event of default, Landlord may pursue any other remedy now or hereafter available to Landlord under the laws or judicial decisions of the State in which the Premises is located. All rights and remedies of Landlord hereunder shall be cumulative and in addition to all rights and remedies given to Landlord at law or equity.

26. LATE CHARGE

If any installment of Rent or other amount owed to Landlord is not paid when due, such amount shall bear interest at the prevailing interest rate from the date on which said payment shall be due until the date on which Landlord shall receive said payment. This provision shall not relieve Tenant of Tenant's obligation to pay Rent at the time and in the manner herein specified.

27. LANDLORD DEFAULT

Landlord shall be in default under this Lease in the event Landlord has not begun and pursued with reasonable diligence the cure of any failure of Landlord to meet its obligations under this Lease within thirty (30) days of the receipt by Landlord of written notice from Tenant of Landlord's alleged failure to perform (and an additional reasonable time after such receipt if (i) such failure cannot reasonably be cured within such thirty (30)-day period, and (ii) Landlord commences curing such failure within such thirty (30)-day period and thereafter diligently pursues the curing of such failure). In addition, Tenant shall prior to the exercise of any such remedies, provide each Landlord's mortgagee (in each instance, only as to those entities of which Tenant has notice of their interest) with written notice and reasonable time to cure any default by Landlord.

28. TENANT'S REMEDIES

In the event Landlord does not cure Landlord's default as provided in this Lease, Tenant may terminate this Lease with no further force and effect upon providing Landlord with thirty (30) calendar days written notice to Landlord no sooner than thirty (30) calendar days after Landlord's receipt or rejection of written notice from Tenant of the need for Landlord to cure the default. In the event Tenant does elect to terminate this Lease pursuant to this Section, Landlord shall reimburse Tenant within thirty (30) calendar days of Landlord's receipt of written notice for the unamortized value (using a straight-line amortization schedule over the Lease Term) of the cost of Tenant's improvements and other costs incurred by Tenant. The withholding, deducting or offsetting by Tenant, or failure to pay Rent by Tenant, pursuant to a bona fide dispute between Landlord and Tenant shall not be deemed a default by Tenant under the provisions of this Lease. The liabilities of Landlord to Tenant for any default by Landlord under the terms of this Lease are not personal obligations of the individual or other partners, directors, officers and shareholders of Landlord, Landlord's wholly-owned subsidiaries or Landlord's agents or operators, and Tenant agrees to look solely to Landlord's interest in the Premises for the recovery of any amount from Landlord, and shall not look to other assets of Landlord, Landlord's wholly-owned subsidiaries or Landlord's agents or operators nor seek recourse against the assets of the individual or other partners, directors, officers and shareholders of Landlord, Landlord's wholly-owned subsidiaries or Landlord's agents or operators. Any lien obtained to enforce any such judgment and any levy of execution thereon shall be subject and subordinate to any lien, mortgage or deed of trust on the Premises.

29. TRANSFERS BY LANDLORD

In the event of a sale or conveyance by Landlord of the Premises or a foreclosure by any creditor of Landlord, the same shall operate to release Landlord from any liability upon any of the covenants or conditions, express or implied, herein contained in favor of Tenant, to the extent required to be performed after the passing of title to Landlord's successor-in-interest. In such event, Tenant agrees to look solely to the responsibility of the successor-in-interest of Landlord under this Lease with respect to the performance of the covenants and duties of Landlord to be performed after the passing of title to Landlord's successor-in-interest. This Lease shall not be affected by any such sale and Tenant agrees to attorn to the purchaser or assignee. Landlord's successor(s)-in-interest shall not have liability to Tenant with respect to the failure to perform all

of the obligations of Landlord, to the extent required to be performed prior to the date such successor(s)-in-interest became the owner of the Premises.

30. RIGHT OF LANDLORD TO PERFORM TENANT'S COVENANTS

All covenants and agreements to be performed by Tenant under any of the terms of this Lease shall be performed by Tenant at Tenant's sole cost and expense and without any abatement of Rent. If Tenant shall fail to pay any sum of money, other than Base Rent and Basic Operating Cost, required to be paid by Tenant hereunder, or shall fail to perform any other act on Tenant's part to be performed hereunder (including without limitation, Tenant's maintenance and repair obligations), and such failure shall continue for ten (10) business days after written notice thereof by Landlord (except that no notice shall be required in case of an emergency), Landlord may, but shall not be obligated to do so, and without waiving or releasing Tenant from any obligation of Tenant, make any such payment or perform any such act on Tenant's part to be made or performed.

31. HAZARDOUS MATERIALS

31.1 **Stored Products Chart**. Prior to executing this Lease, Tenant has delivered to Landlord Tenant's completed Stored Products Chart in the form attached hereto as Exhibit E (the "**Stored Products Chart**"). Tenant covenants, represents and warrants to Landlord that the information in the Stored Products Chart including any attached Material Safety Data Sheet ("**MSDS**") is true and correct and accurately describes the use(s) of Hazardous Materials (as defined below) which will be made and/or used on the Premises by Tenant. Landlord consents to Tenant's storage, use and disposal of said Hazardous Materials in compliance with Environmental Laws (as defined below). Tenant shall, within ten (10) business days of Landlord's request, execute and deliver to Landlord an updated Stored Products Chart in a similar form describing Tenant's then present use of Hazardous Materials on the Premises, and any other reasonably necessary documents, charts or information requested by Landlord with respect to Tenant's use, generation, storage, transportation or disposal of Hazardous Materials.

31.2 **Compliance with Laws and Permits**. During the Term of this Lease, Tenant shall comply with all Environmental Laws and Environmental Permits (each as defined below) applicable to the operation, use or occupancy of the Premises by Tenant, 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 Tenant's operation or use of the Premises. Without limiting the generality of the foregoing, Tenant shall not cause or permit any violation of Environmental Laws or Environmental Permits, including with respect to soil and ground water conditions provided, however, Tenant shall have no obligations with respect to Existing Environmental Conditions. Tenant shall, at Tenant's sole cost, make all submissions to, provide all information required by, and comply with all requirements of, all governmental authorities under Environmental Laws applicable to Tenant.

31.3 **Limitations on Use**. Tenant shall not generate, use, treat, store, handle, manufacture, refine, produce, process, release or dispose of, or permit the generation, use, treatment, storage, handling, manufacture, refinement, production, processing, release or disposal of, Hazardous Materials on, under or about the Premises or the Premises, or transport or permit the

transportation of Hazardous Materials to or from the Premises except for (i) those materials and products utilized in the normal course of Tenant's business and (ii) limited quantities of household cleaning products and office supplies used or stored at the Premises and required in connection with the routine operation and maintenance of the Premises, and in each case used, stored, transported and disposed of in compliance with all applicable Environmental Laws and Environmental Permits.

31.4 **Site Assessments**. At any time and from time to time during the Term of this Lease, Landlord may, with thirty (30) days' notice to Tenant, 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 first brought onto the Premises by Tenant. 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 or any of Tenant's Parties, then such report shall be at Tenant's sole cost and expense, and the cost of such assessment shall be due and payable within thirty (30) days of receipt of an invoice therefor.

31.5 **Notices to Landlord**. Except with respect to Existing Environmental Conditions and environmental matters located below, above or related to Premises but not caused by Tenant, Tenant will immediately advise Landlord in writing of any of the following: (1) any known pending or threatened Environmental Claim (as defined in Section 31(h) below) against Tenant relating to the Premises; (2) any condition or occurrence on the Premises that (i) results in noncompliance by Tenant with any applicable Environmental Law, or (ii) 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 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 caused by Tenant. 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 party relating to Environmental Claims, and such detailed reports of any such Environmental Claim as may reasonably be requested by Landlord.

31.6 **Cleanup Plan**. Should any governmental authority or any third party demand that a cleanup plan be prepared by Tenant and that a cleanup be undertaken because of any deposit, spill, discharge, or other release of Hazardous Materials by Tenant that occurs during the Term of this Lease, at or from the Premises, or which arises at any time from Tenant's use or occupancy of the Premises, then Tenant shall, at Tenant's sole cost, prepare and submit the required plans and all related financial assurances, and Tenant shall carry out all such cleanup plans; provided, however, Tenant shall have no obligations with respect to Existing Environmental

Conditions and environmental matters coming from above, below or related to the Premises and not caused by Tenant.

31.7 **Indemnity**.

(a) Except with respect to Existing Environmental Conditions and environmental matters located above, below or related to Premises and/or not caused by Tenant, Tenant shall indemnify, defend and hold harmless the Landlord Indemnitees and their respective officers, directors, beneficiaries, shareholders, partners, agents and employees, from and against all obligations (including removal and remedial actions), losses, claims, suits, judgments, actions, procedures, liabilities, penalties, fines, damages (including consequential and punitive damages), costs and expenses (including 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 Landlord Indemnitees and their respective officers, directors, beneficiaries, shareholders, partners, agents and employees directly or indirectly based on, or arising or resulting from (i) the actual presence of Hazardous Materials on the Premises which is caused or permitted by Tenant or any of Tenant's Parties, including any deposit, spill, discharge or other release of Hazardous Materials that occurs during the Term at or from the Premises by Tenant or any Tenant Parties; (ii) any Environmental Claim relating to Tenant's operation, use or occupancy of the Premises; or (iii) Tenant's failure to provide information, make all submissions, and take steps required by all governmental authorities under applicable Environmental Laws. The foregoing indemnity shall not include any Existing Environmental Conditions, environmental matters located above, below or related to the Premises and not caused by Tenant or any Hazardous Materials that were located at, on, from, migrating onto or from the Premises or the Premises on or before the Term Commencement Date, or any Hazardous Materials placed on the Premises or the Premises by Landlord, its employees, agents or contractors or any other party other than Tenant or any of Tenant's Parties.

(b) Landlord shall indemnify, defend and hold harmless the Tenant Indemnitees and their respective officers, directors, beneficiaries, shareholders, partners, agents and employees, from and against all obligations (including removal and remedial actions), losses, claims, suits, judgments, actions, procedures, liabilities, penalties, fines, damages (including consequential and punitive damages), costs and expenses (including 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 Tenant Indemnitees and their respective officers, directors, beneficiaries, shareholders, partners, agents and employees directly or indirectly based on, or arising or resulting from Existing Environmental Conditions, environmental matters located above, below or related to the Premises and not caused by Tenant's business or Hazardous Materials in any way connected with or alleged or claimed to arise out of, result from or be in any way connected with (a) the use or occupancy of the Premises by the Landlord or any previous owner/occupant/user of the Premises, or any portion thereof, prior to Tenant's occupancy of the Premises; (b) the use or occupancy of the Premises by any subsequent owner/occupant/user of the Premises, or any portion thereof, after Tenant's occupancy of the Premises terminates; (c) violations by any prior or subsequent owner/ occupant/user of the Premises of local, state and/ or federal laws and regulations, including all applicable Environmental Laws and regulations as well as any liabilities resulting from the practices of the prior or subsequent owner/ occupant/ user whether or not such practices were or could be deemed a violation of such laws and regulations;

and (d) contamination of the Premises by Landlord or by its agents or employees during the term hereof. The foregoing indemnity shall not include any Hazardous Materials that were first caused or permitted by Tenant or any of Tenant's Parties after the Term Commencement Date, including without limitation any deposit, spill, discharge or other release of Hazardous Materials by Tenant or Tenant Parties that occurs during the Term at or from the Premises.

31.8 **Landlord's Right to Perform**. If Tenant fails to fulfill any duty imposed under this Section 31 within a reasonable time, Landlord may do so; and in such case, Tenant shall cooperate with Landlord in order to prepare all documents Landlord deems necessary or appropriate to determine the applicability of Environmental Laws to the Premises and Tenant's use thereof, and for compliance therewith, and Tenant shall execute all documents promptly upon Landlord's request. No such action by Landlord and no attempt made by Landlord to mitigate damages under any Environmental Law shall constitute a waiver of any of Tenant's obligations under this Section 31.

31.9 **Defined Terms**. (a) "**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; (iii) any substance that is flammable, explosive, radioactive, noxious or otherwise dangerous or potentially dangerous; (iv) any carcinogenic substance; (v) any other substance exposure to which is regulated by any governmental authority; or (vi) any other substance the removal of which is required, or the manufacture, preparation, production, generation, use, maintenance, treatment, storage, transfer, handling or ownership of which is restricted, prohibited, regulated or penalized by any Environmental Law; (b) "**Environmental Law**" means any federal, state, county or municipal statute, law, rule, regulation, ordinance, code, policy or rule of common law now or hereafter in effect and in each case as amended or supplemented, 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 Federal Water Pollution Control Act, 33 U.S.C. §§ 1251 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., as all of the foregoing laws have been amended or supplemented; (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; and (e) "**Existing Environmental Conditions**" means any Hazardous Materials present at, on, below, migrating from or to the Premises prior to or as of the Term Commencement Date, including but not limited to Hazardous Materials and environmental conditions described or referenced in any documents referenced in Exhibit B.

Survival. The provisions of this Section 31 shall survive the expiration or sooner termination of this Lease.

32. WAIVER

If either Landlord or Tenant waives the performance of any term, covenant or condition contained in this Lease, such waiver shall not be deemed to be a waiver of any subsequent breach of the same or any other term, covenant or condition contained herein. The acceptance of Rent by Landlord shall not constitute a waiver of any preceding breach by Tenant of any term, covenant or condition of this Lease, regardless of Landlord's knowledge of such preceding breach at the time Landlord accepted such Rent. Failure by Landlord to enforce any of the terms, covenants or conditions of this Lease for any length of time shall not be deemed to waive or to decrease the right of Landlord to insist thereafter upon strict performance by Tenant. Waiver by Landlord of any term, covenant or condition contained in this Lease may only be made by a written document signed by Landlord.

33. SURRENDER OF PREMISES

33.1 Prior to the expiration or sooner termination of this Lease, the Parties shall have a Phase I/II environmental assessment test ("**Exit Environmental Assessment**") performed and a complete an accurate copy provided to each Party. Tenant shall be responsible for the costs of the Phase I/II environmental assessment tests.

33.2 Upon the expiration or sooner termination of this Lease, Tenant shall surrender the Premises to Landlord, "broom clean" and without debris, with all specialty Tenant Improvements, machinery, equipment, furnishings and personal property removed therefrom, except for ordinary wear and tear which Tenant was not otherwise obligated to remedy under any provision of this Lease. The Parties agree that "**ordinary wear and tear**" means that there will be a gradual deterioration in condition resulting from Tenant's normal use during the course of Tenant's business over the Term. Prior to Tenant taking possession of the Premises, Landlord shall accurately document the condition Premises (the "**Condition Documentation**"), including equipment and fixtures, and shall provide a copy of the Condition Documentation prior to Tenant taking possession of the Premises. In the event that Landlord fails to provide the Condition Documentation to Tenant prior to Tenant taking possession of the Premises, the condition of the Premises shall be deemed to not exceed ordinary wear and tear. However, Tenant shall not be obligated to repair any damage which Landlord is required to repair under Sections 22 and 23. All Alterations which Landlord has not required Tenant to remove shall become Landlord's property and shall be surrendered to Landlord upon the termination of the Lease, except that Tenant may

remove (and shall remove if so required by Landlord) any of Tenant's machinery or equipment which can be removed without material damage to the Premises. Tenant shall repair, at Tenant's expense, any damage to the Premises caused by the removal of any such machinery or equipment. In no event, however, shall Tenant remove any of the following materials or equipment without Landlord's prior written consent: any power wiring or power panels; lighting or lighting fixtures; wall coverings; drapes, blinds or other window coverings; carpets or other floor coverings; heaters, air conditioners or any other HVAC equipment; fencing or security gates; or other similar building operating equipment and decorations. Tenant shall use commercially reasonable efforts to provide Landlord written notice at least thirty (30) days' prior to vacating the Premises and shall meet with Landlord for a joint inspection of the Premises at the time of vacating. In the event of Tenant's failure to participate in such joint inspection, Landlord shall make commercially reasonable attempts to schedule an inspection with Tenant at or after Tenant vacates the Premises, but in no event later than ten (10) business days after vacating the Premises, and the parties shall come to an agreement for repairs and restoration.

34. NOTICES

All notices, demands, consents and approvals which may or are required to be given by either party to the other hereunder shall be in writing and either personally delivered, sent by commercial overnight courier, or mailed, certified or registered, postage prepaid, and addressed to the party to be notified at the address(es) for such party as specified in the Basic Lease Information or to such other place as the party to be notified may from time to time designate by at least fifteen (15) days' notice to the other party. Notices shall be deemed served upon receipt or refusal to accept delivery.

35. ATTORNEYS' FEES

In the event that Landlord places the enforcement of this Lease, or any part thereof, or the collection of any Rent due, or to become due hereunder, or recovery of possession of the Premises in the hands of an attorney, Tenant shall pay to Landlord, upon demand, Landlord's reasonable attorneys' fees and court costs. In any action which Landlord or Tenant brings to enforce its respective rights hereunder, the unsuccessful party shall pay all costs incurred by the prevailing party including reasonable attorneys' fees, to be fixed by the court, and said costs and attorneys' fees shall be a part of the judgment in said action. Tenant shall pay Landlord's reasonable attorneys' fees incurred in connection with Tenant's request for Landlord's consent under Section 21 or in connection with any other act which Tenant proposes to do and which requires Landlord's consent.

36. AUTHORITY OF PARTIES

Landlord represents and warrants that it has full right and authority to enter into this Lease and to perform all of Landlord's obligations hereunder. Tenant represents and warrants that it has full right and authority to enter into this Lease and to perform all of Tenant's obligations hereunder.

37. SUCCESSORS AND ASSIGNS

This Lease shall be binding upon and inure to the benefit of Landlord, its successors and assigns, and shall be binding upon and inure to the benefit of Tenant, its heirs, successors, and to the extent assignment is approved by Landlord hereunder, Tenant's assigns.

38. FORCE MAJEURE

Whenever a period of time is herein prescribed for action to be taken by Landlord, Landlord shall not be liable or responsible for, and there shall be excluded from the computation for 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 Landlord.

39. BROKERAGE COMMISSION

Landlord shall not be obligated to pay a brokerage commission to the Broker identified in the Basic Lease Information Tenant and Landlord warrant to each other that their contact with the other in connection with this transaction has been through such Broker, and that no other broker or finder can properly claim a right to a commission or a finder's fee based upon contacts between the claimant and Tenant and/or Landlord with respect to the leasing of the Premises.

40. WAIVER OF TRIAL BY JURY

LANDLORD AND TENANT HEREBY KNOWINGLY, VOLUNTARILY AND INTENTIONALLY WAIVE THE RIGHT TO A TRIAL BY JURY IN RESPECT OF ANY LITIGATION BASED HEREON, ARISING OUT OF, UNDER OR IN CONNECTION WITH THIS LEASE OR ANY DOCUMENTS CONTEMPLATED TO BE EXECUTED IN CONNECTION HEREWITH OR ANY COURSE OF CONDUCT, COURSE OF DEALINGS, STATEMENTS (WHETHER ORAL OR WRITTEN) OR ACTIONS OF EITHER PARTY ARISING OUT OF OR RELATED IN ANY MANNER. TO THE PREMISES (INCLUDING WITHOUT LIMITATION, ANY ACTION TO RESCIND OR CANCEL THIS LEASE OR ANY CLAIMS OR DEFENSES ASSERTING THAT THIS LEASE WAS FRAUDULENTLY INDUCED OR IS OTHERWISE VOID OR VOIDABLE). THIS WAIVER IS A MATERIAL INDUCEMENT FOR LANDLORD TO ENTER INTO AND ACCEPT THIS LEASE, AND SHALL SURVIVE THE EXPIRATION OR EARLIER TERMINATION OF THIS LEASE.

41. ACCESSIBILITY INSPECTION DISCLOSURE

Pursuant to California Civil Code section 1938, Landlord provides the following disclosure:

"As of the date of execution of this Lease, the Premises (Check one):

☐ has undergone inspection by a Certified Access Specialist and has been determined to meet all applicable construction-related accessibility standards pursuant to California Civil Code section 55.53.
☐ has undergone inspection by a Certified Access Specialist and has been determined not to meet all applicable construction-related accessibility standards pursuant to California Civil Code section 55.53.

☐ has not undergone inspection by a Certified Access Specialist. Please be advised: "A Certified Access Specialist (CASp) can inspect the subject premises and determine whether the subject premises comply with all of the applicable construction-related accessibility standards under state law. Although state law does not require a CASp inspection of the subject premises, the commercial property owner or lessor may not prohibit the lessee or tenant from obtaining a CASp inspection of the subject premises for the occupancy or potential occupancy of the lessee or tenant, if requested by the lessee or tenant. The parties shall mutually agree on the arrangements for the time and manner of the CASp inspection, the payment of the fee for the CASp inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the premises."

42. MISCELLANEOUS

42.1 **General**. The term "Tenant" or any pronoun used in place thereof shall indicate and include the masculine or feminine, the singular or plural number, individuals, firms or corporations, and their respective successors, heirs, executors, administrators and permitted assigns, according to the context hereof.

42.2 **Time**. Time is of the essence regarding this Lease and all of its provisions.

42.3 **Choice of Law**. The laws of the State in which the Premises is located shall in all respects govern this Lease.

42.4 **Exhibits**. The Exhibits attached hereto are hereby incorporated herein by this reference.

42.5 **Entire Agreement**. This Lease, together with its Exhibits, contains all the agreements of the parties hereto and supersedes any previous negotiations. There have been no representations made by Landlord or understandings made between the parties other than those set forth in this Lease and its Exhibits.

42.6 **Modifications**. This Lease may not be modified except by a written instrument signed by the parties hereto.

42.7 **Severability**. If, for any reason whatsoever, any of the provisions hereof shall be unenforceable or ineffective, all of the other provisions shall be and remain in full force and effect.

42.8 **Examination of Lease**. Submission of this Lease to Tenant does not constitute an option or offer to lease and this Lease is not effective otherwise until execution and delivery by both Landlord and Tenant.

42.9 **Accord and Satisfaction**. No payment by Tenant of a lesser amount than the Rent due nor any endorsement on any check or letter accompanying any check or payment of Rent shall be deemed an accord and satisfaction of full payment of Rent, and Landlord may accept such payment without prejudice to Landlord's right to recover the balance of such Rent or to pursue other remedies.

42.10 **Joint and Several Liability**. All parties signing this Lease as Tenant shall be jointly and severally liable for all obligations of Tenant.

42.11 **Easements**. Landlord may grant easements on or over the Premises and dedicate for public use portions of the Premises with Tenant's consent and no such grant or dedication shall substantially interfere with Tenant's use of or access to the Premises. Upon Landlord's demand, Tenant shall execute, acknowledge and deliver to Landlord documents, instruments, maps and plats necessary to effectuate Tenant's covenants hereunder.

42.12 **Drafting and Determination Presumption**. The parties acknowledge that both parties have agreed to this Lease, that both Landlord and Tenant have consulted with attorneys with respect to the terms of this Lease, and that no presumption shall be created against Landlord because Tenant shall be deemed to have drafted this Lease. Except as otherwise specifically set forth in this Lease, with respect to any consent, determination or estimation of Landlord required in this Lease or requested of Landlord, Landlord's consent, determination or estimation shall be made in Landlord's good faith opinion, whether objectively reasonable or unreasonable.

42.13 **Execution of Lease**. This Lease may be executed in counterparts, and, when all counterpart documents are executed, the counterparts shall constitute a single binding instrument.

42.14 **No Light, Air or View Easement**. Any diminution or shutting off of light, air or view by any structure which may be erected on lands adjacent to or in the vicinity of the Premises shall in no way affect this Lease or impose any liability on Landlord.

42.15 **No Third Party Benefit**. This Lease is a contract between Landlord and Tenant and nothing herein is intended to create any third-party benefit.

42.16 **Non-Discrimination**. Tenant hereby covenants to Landlord, and it is a condition to the continuance of this Lease, that there will be no discrimination against, or segregation of, any person or group of persons on the basis of race, color, sex, creed, national origin or ancestry in the leasing, subleasing, transferring, occupancy or use of the Premises or any portion thereof.

42.17 **OFAC Restrictions**. Tenant warrants and represents to Landlord that Tenant is not, and shall not become, a person or entity with whom Landlord is restricted from doing business under regulations of the Office of Foreign Asset Control ("**OFAC**") of the Department of

the Treasury (including, but not limited to, those named on OFAC'S Specially Designated and Blocked Persons list) or under any statute, executive order (including, but not limited to, the September 24, 2001 Executive Order Blocking Property and Prohibiting Transactions With Persons Who Commit, Threaten to Commit, or Support Terrorism), or other governmental action, and is not and shall not engage in any dealings or transaction or be otherwise associated with such persons or entities.

43. OPTION TO EXTEND LEASE

43.1 **Option to Extend Lease Term.** Tenant shall have the right to renew this Lease ("**Option To Extend Lease**") for two (2) five (5) year periods (each an "**Option To Extend Lease**") subject to the terms and conditions as set forth in this Section 43.

43.2 **Exercise of Option To Extend Lease.** Tenant shall exercise the Option To Extend Lease, if at all, by giving Landlord written notice of Tenant's intention to do so at least six (6) months prior to the expiration of the original Term, time being of the essence herein. Notwithstanding the foregoing, Tenant shall not have the right to exercise the Option To Extend Lease if Tenant is in material default under this Lease at the time of the purported exercise of Option to Extend Lease. The Option To Extend Lease Term shall be upon all of the terms and conditions of this Lease, except that the monthly Base Rent for such Option To Extend Lease Term shall be determined in accordance with subsection (c) herein below. The extension of the Term shall be on an "AS IS" basis. Upon commencement of the Option To Extend Lease Term, all references herein to the "Lease Term" of this Lease shall be deemed to include the Option To Extend Lease Term. Unless expressly mentioned and approved in the written consent of Landlord provided for by Section 21 of this Lease, Tenant's Option To Extend Lease right is granted for Tenant's personal benefit and may not be assigned or transferred by Tenant.

43.3 **Option To Extend Lease Term Base Rent.** Base Rent for each Option To Extend Lease Term shall be at one hundred percent (100%) of the then fair market value (FMV) which shall be as determined as follows:

(a) Within thirty (30) days after Landlord's receipt of Tenant's notice of exercise of the Option To Extend Lease, Landlord shall deliver to Tenant a proposal setting forth the monthly Base Rent for the Option To Extend Lease Term, including annual increases, if applicable. Landlord's proposal shall be based upon the fair market rental for the Premises based on properties similar to the Premises' condition at the execution of the Option to Extend Lease . If Tenant, within ten (10) business days after receipt of such proposal, agrees to the Base Rent proposed by Landlord, or fails to notify Landlord of its acceptance or rejection of such proposal (in which event Tenant shall be deemed to have agreed thereto), the amount of monthly Base Rent set forth in such proposal shall be binding upon Landlord and Tenant. Should Tenant object in writing to Landlord's proposal within ten (10) business days after receipt thereof, then during the fifteen (15) day period following Tenant's objection to Landlord's proposal, Landlord and Tenant shall negotiate in good faith for the purpose of reaching an agreement on the Base Rent amount. In the event the parties fail to agree in a written instrument signed by both parties within such fifteen (15) day period, the monthly Base Rent shall be determined by appraisal in the manner set forth in subparagraph (d) herein below; provided, however, that in no event shall the monthly Base

Rent for the Option To Extend Lease Term be less than the monthly Base Rent payable hereunder for the last full month of the original Term. For the purposes of the preceding sentence, the amount of monthly Base Rent for the last month of the Lease shall not be reduced to reflect any abatement of Base Rent which may then be in effect.

43.4 **Appraisal.** In the event it becomes necessary to determine the fair market monthly Base Rent by appraisal hereunder, then within fifteen (15) days following the fifteen (15) day period referenced in subsection (c)(i) herein above, Landlord and Tenant each shall appoint a real estate appraiser who shall be a member of the American Institute of Real Estate Appraisers ("**AIREA**"), or comparable professional organization for appraisers, with at least ten (10) years' commercial appraisal experience in the area in which the Premises is located, and such appraisers shall each determine the fair market monthly Base Rent, including annual increases, if applicable, taking into account the value of the Premises and prevailing comparable rentals in the same geographical area as the Premises. Such appraisers shall, within twenty (20) days after their appointment, complete their appraisals and submit their appraisal reports to Landlord and Tenant. If the fair market monthly Base Rent for the Premises established in the two (2) appraisals varies by less than five percent (5%) of the higher rental, the two (2) appraisals shall be averaged and the resulting amount shall be the Base Rent for the Premises. If, however, the fair market monthly Base Rent for the Premises established by the two (2) appraisals varies by five percent (5%) or more of the higher rental, said appraisers, within ten (10) days after submission of the last appraisal, shall appoint a third appraiser who shall be a member of the AIREA, or comparable professional organization for appraisers, with comparable experience and who has not previously represented either party. Such third-party appraiser shall, within twenty (20) days after his or her appointment, determine by appraisal the fair market monthly Base Rent for the Premises, taking into account the same factors referred to above, and submit his or her appraisal report to Landlord and Tenant. The fair market monthly Base Rent determined by the third appraiser for the Premises shall be controlling. If either Landlord or Tenant fails to appoint an appraiser, or if an appraiser appointed by either of them fails, after his or her appointment, to submit his or her appraisal within the required time period in accordance with the foregoing, the appraisal submitted by the appraiser properly appointed and timely submitting his or her appraisal shall be controlling. If the two (2) appraisers appointed by Landlord and Tenant are unable to agree upon a third appraiser within the required period in accordance with the foregoing, application shall be made within twenty (20) days thereafter by either Landlord or Tenant to the AIREA, or comparable professional organization for appraisers, which shall appoint a member of said institute willing to serve as appraiser. The cost of all appraisals under this subsection (d) shall be borne equally by Landlord and Tenant.

43.5 **Amendment to Lease**. The new Base Rent established for the Extended Term shall be promptly memorialized by the parties in an amendment or letter agreement prepared by Landlord.

[END OF GENERAL LEASE TERMS]

Exhibit 21.1

Significant Subsidiaries of Ultragenyx Pharmaceutical Inc.

Name of Subsidiary	Jurisdiction of Incorporation
Ultragenyx Holdco LLC	Delaware
Ultragenyx UK Ltd	United Kingdom
Ultragenyx Europe GmbH	Switzerland
Ultragenyx Germany GmbH	Germany
Ultragenyx Brasil Farmacêutica Ltda	Brazil
Ultragenyx Argentina SRL	Argentina
Ultragenyx Netherlands B.V.	Netherlands
Ultragenyx France SAS	France
Ultragenyx Colombia SAS	Colombia
Ultragenyx Canada Inc.	Canada
Ultragenyx México, S. de R.L. de C.V.	Mexico

Exhibit 23.1

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. 333-223123) of Ultragenyx Pharmaceutical Inc.,

(2) Registration Statements (Form S-8 Nos. 333-194773, 333-201843, 333-209729, 333-216110, 333-223124 and 333-229746) pertaining to the 2011 Equity Incentive Plan, as amended, 2014 Incentive Plan and 2014 Employee Stock Purchase Plan of Ultragenyx Pharmaceutical Inc., and

(3) Registration Statement (Form S-8 No. 333-221381) pertaining to the Dimension Therapeutics, Inc. 2015 Stock Option and Incentive Plan and the Dimension Therapeutics, Inc. 2013 Stock Plan, both as assumed by Ultragenyx Pharmaceutical Inc.;

of our reports dated February 13, 2020, 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, 2019.

/s/ Ernst & Young LLP

San Jose, California
February 13, 2020

Exhibit 31.1

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 the 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 13, 2020

/s/ Emil D Kakkis

Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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 the 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 13, 2020

/s/ Shalini Sharp
Shalini Sharp
Chief Financial Officer and Executive Vice President
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO SECTION 906 OF
THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. SECTION 1350)

In connection with the accompanying Annual Report of Ultragenyx Pharmaceutical Inc. (the "Company") on Form 10-K for the year ended December 31, 2019 (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 Executive 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 13, 2020

/s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: February 13, 2020

/s/ Shalini Sharp
Shalini Sharp
Chief Financial Officer and Executive Vice President
(Principal Financial Officer)