**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, 2022**
**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**<br>**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 Exchange Act:**

| Title of each class | Trading Symbol(s) | 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 Exchange 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 Exchange 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 Exchange Act 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 an 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☑

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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Company as of June 30, 2022 was approximately $3.3 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 as such persons may be deemed affiliates of the Company. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 13, 2023, the Company had 70,216,689 shares of common stock issued and outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive proxy statement relating to its 2023 Annual Meeting of Stockholders, to be held on or about June 7, 2023, 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 fact 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;
- the impact of the COVID-19 pandemic and related health measures on our business, financial condition and liquidity;
- 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;
- stagnating or worsening business and economic conditions and increasing geopolitical instability, including inflationary pressures, general economic slowdown or a recession, rising interest rates, foreign exchange rate volatility, and changes in monetary policy; 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 refer to 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 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 biologics, small molecules, gene therapy, and nucleic acids provide us with what we believe is an optimal set of options to treat 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.
- ***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 throughout the developed world, in North America, the European Union, or the EU, the United Kingdom, or the U.K., Latin America, Turkey, Asia, 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.

**Approved Products and Clinical Product Candidates**

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

We have four commercially approved products, Crysvita® (burosumab) for the treatment of X-linked hypophosphatemia, or XLH, and tumor-induced osteomalacia, or TIO, Mepsevii® (vestronidase alfa) for the treatment of mucopolysaccharidosis VII, or MPSVII or Sly Syndrome, Dojolvi® (triheptanoin) for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD, and Evkeeza® (evinacumab) for the treatment of homozygous familial hypercholesterolemia, or HoFH. The following table summarizes our approved products and clinical product candidate pipeline:

| Products | Description | Indication | Therapeutic Area | IND Stage[1] | Phase 1 | Phase 2 | Phase 3 | Approved |
|---|---|---|---|---|---|---|---|---|
| **Biologics** | | | | | | | | |
| **Crysvita® (burosumab)[2]** | Anti-FGF23 monoclonal antibody | XLH | Bone / Endocrine | | | | | |
| **Crysvita® (burosumab)[2]** | Anti-FGF23 monoclonal antibody | TIO | Bone / Endocrine | | | | | |
| **Mepsevii® (vestronidase alfa)** | Enzyme replacement | MPSVII | Metabolics | | | | | |
| **Evkeeza® (evinacumab)[3]** | Fully human monoclonal antibody | HoFH | Metabolics | | | | | |
| **UX143 (setrusumab)[4]** | Fully human monoclonal antibody | OI | Bone / Endocrine | | | | | |
| **Small Molecules** | | | | | | | | |
| **Dojolvi® (triheptanoin)** | Substrate replacement | LC-FAOD | Metabolics | | | | | |
| **AAV Gene Therapy** | | | | | | | | |
| **UX111** | AAV9 Gene Therapy | MPS IIIA | CNS / Muscle | | | | | |
| **DTX401** | AAV8 Gene Therapy | GSDIa | Metabolics | | | | | |
| **DTX301** | AAV8 Gene Therapy | OTC | Metabolics | | | | | |
| **UX701** | AAV9 Gene Therapy | Wilson | Metabolics | | | | | |
| **Nucleic Acid** | | | | | | | | |
| **GTX-102** | Antisense Oligonucleotide | Angelman Syndrome | CNS / Muscle | | | | | |
| **UX053** | mRNA | GSDIII | Metabolics | | | | | |

1: IND submitted or expected to be submitted within the near term
2: In collaboration with Kyowa Kirin Company
3: Ex-US collaboration with Regeneron Pharmaceuticals
4: In collaboration with Mereo BioPharma

**Approved Products**

***Crysvita for the treatment of XLH and TIO***

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 U.S., the EU and certain other regions for the treatment of XLH in adult and pediatric patients one year of age and older.

Crysvita is also approved in the U.S. and certain other regions for the treatment of FGF23-related hypophosphatemia in tumor-induced osteomalacia, or TIO, associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older. There are approximately 2,000 to 4,000 patients with TIO in the developed world. TIO can lead to severe hypophosphatemia, osteomalacia, fractures, fatigue, bone and muscle pain, and muscle weakness.

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.

Please see "—License and Collaboration Agreements—Approved Products—Kyowa Hakko Kirin" for a description of our collaboration and license agreement with 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 U.S., the EU and certain other regions for the treatment of children and adults with MPS VII.

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

***Dojolvi for the treatment of LC-FAOD***

Dojolvi is a highly purified, synthetic, 7-carbon fatty acid triglyceride specifically designed to provide medium-chain, odd-carbon fatty acids as an energy source and metabolite replacement for people with long-chain fatty acid oxidation disorders, or 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. Dojolvi is approved in the U.S. and certain other regions as a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed LC-FAOD. There are approximately 8,000 to 14,000 patients in the developed world with LC-FAOD.

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

***Evkeeza for the treatment of HoFH***

Evkeeza is a fully human monoclonal antibody that binds to and blocks the function of angiopoietin-like 3, or ANGPTL3, a protein that plays a key role in lipid metabolism. Evkeeza is an approved therapy for the treatment of homozygous familial hypercholesterolemia, or HoFH, a rare inherited condition. HoFH occurs when two copies of the familial hypercholesterolemia, or FH,-causing genes are inherited, one from each parent, resulting in dangerously high levels (>400 mg/dL) of LDL-C, or bad cholesterol. Patients with HoFH are at risk for premature atherosclerotic disease and cardiac events as early as their teenage years. Evkeeza is approved in the U.S., where it is marketed by our partner Regeneron Pharmaceuticals, or Regeneron. It is also approved in the European Economic Area, or EEA, as a first-in-class therapy for use together with diet and other low-density lipoprotein-cholesterol, or LDL-C, lowering therapies to treat adults and adolescents aged 12 years and older with clinical HoFH. There are approximately 3,000 to 5,000 patients with HoFH in the developed world outside of the U.S.

In January 2022, we announced a collaboration with Regeneron to commercialize Evkeeza outside of the U.S. We are in the process of engaging country authorities within the EEA, Latin America, Canada and Japan to negotiate pricing and reimbursement guidelines.

Please see "—License and Collaboration Agreements—Approved Products—Regeneron" for a description of our license agreement with Regeneron Pharmaceuticals.

**Clinical Product Candidates**

***UX143 (setrusumab) for the treatment of Osteogenesis Imperfecta, or OI***

UX143 (setrusumab) is a fully human monoclonal antibody that inhibits sclerostin, a protein that acts on a key bone-signaling pathway by inhibiting the activity of bone-forming cells and promoting bone resorption. Setrusumab is being studied for the treatment of OI, and has received orphan drug designation from the U.S. Food and Drug Administration, or FDA, and European Medicines Agency, or EMA, rare pediatric disease designation from the FDA, and was accepted into the EMA's Priority Medicines program, or PRIME, program. Setrusumab is subject to our collaboration agreement with Mereo, and is the lead clinical asset in our bone endocrinology franchise. There are an estimated 60,000 patients in the developed world affected by OI.

In February 2023, we announced enrollment was completed in the Phase 2 portion of pediatric and young adult Phase 2/3 study. This phase is intended to determine an optimized dose, based on increases in collagen production using serum P1NP levels, and establish an acceptable safety profile. Data from the Phase 2 study and determination of the Phase 3 dose strategy are currently expected mid-2023. We intend to adapt the study into a pivotal Phase 3 stage, evaluating fracture reduction over an estimated 15 to 24 months as the primary endpoint, subject to regulatory review. Separately, we plan to initiate a Phase 2 study of patients under age five with OI in the first half of 2023.

In February 2023, we and our development partner Mereo entered into a non-exclusive worldwide, royalty-free license with UCB Pharma S.A., or UCB, and their partner Amgen Inc., or Amgen, to research, develop, and commercialize setrusumab in OI under certain UCB/Amgen-owned patent rights related to anti-sclerostin compounds and their uses.

Please see “—License and Collaboration Agreements—Clinical Product Candidates—Mereo” for a description of our license and collaboration agreement with Mereo.

***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 caused by loss-of-function of the maternally inherited allele of the UBE3A gene. There are an estimated 60,000 patients in the developed world affected by Angelman syndrome. GTX-102 has received Fast Track Designation, Orphan Drug Designation and Rare Pediatric Disease Designation from the FDA. We exercised our option to acquire GeneTx Biotherapeutics LLC (GeneTx) in July 2022 for an option exercise price of $75.0 million, in addition to outstanding cash and adjustments for working capital, for a total purchase consideration of $91.2 million. Additionally, we may make future milestone and royalty payments to GeneTx.

In July 2022, we provided an interim data update on patients treated in Canada, the U.K., and the U.S. under each region’s amended protocol for the phase 1/2 study of GTX-102. As of the data cut-off for this update, a total of 11 patients had reached at least the Day 128 evaluation, with three patients reaching the Day 170 Pre-Maintenance Dose, or PMD, evaluation. We evaluated patients across various clinical measurements, including AS Change Scale, AS Severity Scale, the Bayley Scales of Infant and Toddler Development, or Bayley-4, the Vineland-3 adaptive behavior scale, and the Observed Reported Communication Ability, or ORCA.

In January 2023, we announced 23 patients had received loading doses ranging from 2 mg to 10 mg, with maintenance dosing ranging from 10 mg to 14 mg. Ten patients have had between six and twelve months of exposure to GTX-102 and five patients have been on continuous therapy for more than one year. To date, the most common adverse events, or AE, have not been related to treatment and include COVID-19 infection, vomiting and upper respiratory infection. In January 2023, we disclosed one AE of special interest that occurred in a 17 year-old patient with severe scoliosis and who had, at baseline, limited ability to walk and was primarily dependent on a wheelchair. After the fourth monthly loading dose this patient experienced decreased ambulation, which clinically resolved within a couple of weeks. As of this filing, there have been no other cases of lower extremity weakness under the amended protocol.

Three of the original five patients treated in the U.S. have successfully restarted therapy with GTX-102. Two of these patients are being treated under the Canadian protocol and one through an early access protocol in the U.S. These patients have showed

signs of clinical activity, including improvements in sleep. As of this filing, there have been no reports of lower extremity weakness in these three patients.

In the U.K. and Canada, dosing is ongoing under a protocol amendment approved in May 2022 that began with lower loading doses and has progressed to incrementally higher loading doses based on age and clinical activity. In the U.S., discussions are currently ongoing with the FDA to harmonize the three regions.

In February 2023, screening began for patients in expansion Cohort A (ages 4 to <8 years) and expansion Cohort B (ages 8 to <18 years). Each expansion cohort will enroll approximately 20 patients and will evaluate the same safety, pharmacokinetic, and efficacy measures as the dose escalating cohorts.

Across the patients who have been dosed under the amended and expanded access protocols, we are continuing to see encouraging signs of clinical activity. We expect to provide the next data update, based on a larger number of patients in the program, later this year.

***UX111 for the treatment of Sanfilippo syndrome type A or MPS IIIA***

UX111 (formerly ABO-102) is an adeno-associated virus 9, or AAV9, gene therapy product candidate for the treatment of patients with Sanfilippo syndrome type A, or MPS IIIA, a rare lysosomal storage disease with no approved treatment, which primarily affects the central nervous system. There are an estimated 3,000 to 5,000 patients in the developed world affected by Sanfilippo syndrome type A. The UX111 program has received Regenerative Medicine Advanced Therapy, or RMAT, Fast Track, Rare Pediatric Disease, and Orphan Drug Designations in the U.S., and PRIME and Orphan Medicinal Product designations in the EU.

In May 2022, we announced an exclusive license agreement with Abeona Therapeutics for UX111. Under the terms of the agreement, we assumed responsibility for the UX111 program in exchange for Abeona's right to receive tiered royalties of up to 10% on net sales, and milestone payments upon the attainment of certain commercial revenue milestones.

Abeona previously announced the completion of a successful Type B meeting with the FDA regarding the pivotal Transpher A trial to support filing and approval for UX111. Interim results from the Transpher A trial presented in an encore presentation at the 2022 American Society of Gene & Cell Therapy, or ASGCT, conference demonstrated that neurocognitive development was preserved in children treated younger than 2 years or in children older than 2 years with a development quotient (DQ) > 60 (n=10) within normal range of a non-afflicted child after treatment with ABO-102 (3.0 x 10^13 vg/kg). The interim results also showed continued or stabilized cognitive function along with behavioral and developmental progress using standard assessments. Additionally, stabilization or increase in volumes of cortical gray matter, total cerebral, and amygdala was observed. Statistically significant reduction in liver volume was seen with UX111 treatment. Dose-dependent and statistically significant reductions in cerebrospinal fluid and plasma heparan sulfate, demonstrating replacement of enzyme activity consistent with levels required for disease correction in the central nervous system, have been sustained in treated patients for two years after treatment. As of the ASGCT presentation, there had been no treatment-related serious adverse events and no clinically meaningful adverse events.

A meeting with the FDA to discuss a plan to file for accelerated approval is expected to occur in the first half of 2023.

***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. GSDIa is the most common genetically inherited glycogen storage disease, with an estimated 6,000 patients in the developed world affected by GSDIa. A Pediatric Investigation Plan, or PIP, was accepted by the EMA. The DTX401 program has received RMAT, Fast Track, and Orphan Drug designations in the U.S., and PRIME and Orphan Medicinal Product Designations in the EU.

In May 2022, we presented longer-term safety and durability data from the ongoing Phase 1/2 study at the ASGCT conference, which showed sustained responses lasting more than 3.5 years following treatment with DTX401. All 12 patients in the study have demonstrated reductions in oral glucose replacement therapy, with a mean total daily reduction of 70% (p-value<0.0001) from baseline to the last available timepoint. At the ASGCT presentation, we also presented data that showed additional improvements of greater time spent in euglycemia and reduced average daily cornstarch intake, as measured by continuous glucose monitoring.

As of January 2023, enrollment in the baseline screening has been completed in the Phase 3 GlucoGene study of DTX401. The Phase 3 study has a 48-week primary efficacy analysis period and enrolled approximately 50 patients eight years of age and older, randomized 1:1 to DTX401 (1.0 x 10^13 GC/kg dose) or placebo. The primary endpoint is the reduction in oral glucose replacement with cornstarch while maintaining glucose control. We currently expect to share results from this Phase 3 study, following the 48-week primary efficacy analysis, in the first half of 2024.

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 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 U.S. and in the EU and Fast Track Designation in the U.S.

In May 2022, we presented additional longer-term safety and durability data from the ongoing Phase 1/2 study at the 2022 ASGCT conference, which showed sustained responses lasting more than 4 years following treatment with DTX301. Seven of 11 patients, including four out of the five patients treated at the Phase 3 dose (1.7 x 10^13 GC/kg), have responded, and remain clinically and metabolically stable. Four complete responders have discontinued ammonia-scavenger medications and liberalized their diet within the first year after treatment. As of May 2022, across all cohorts of the Phase 1/2 study, no treatment-related serious adverse events, infusion-associated reactions or dose-limiting toxicities have been reported.

The Phase 3 Enh3ance study randomized and dosed the first patient earlier this year. Additional patients are currently in the approximate 4- to 8-week baseline screening period, after which they are expected to receive a single dose of DTX301 or placebo. The Phase 3 study will include a 64-week primary efficacy analysis period and we currently plan to enroll approximately 50 patients 12 years of age and older, randomized 1:1 to DTX301 (1.7 x 10^13 GC/kg dose) or placebo. The co-primary endpoints are the percentage of patients who achieve a response, as measured by discontinuation or reduction in baseline disease management, and the 24-hour plasma ammonia levels.

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

***UX701 for the treatment of Wilson Disease***

UX701 is an AAV type 9 gene therapy product candidate designed to deliver stable expression of a truncated version of the ATP7B copper transporter following a single intravenous infusion to patients with Wilson disease. It is estimated that Wilson disease affects more than 50,000 individuals in the developed world. UX701 has received Orphan Drug Designation in the U.S. and in the EU.

UX701 has received a Fast Track Designation from the FDA. This will allow for early and frequent communication throughout the entire drug development and review process and reflects the serious, unmet need for patients with Wilson disease.

We are currently enrolling and dosing patients with Wilson disease in the first stage of the Cyprus2+ study of UX701. During the first stage, the safety and efficacy of up to three dose levels of UX701 will be evaluated over the course of 52 weeks and a dose will be selected for further evaluation in stage 2. The sequential doses to be evaluated are 5.0 x 10^12 GC/kg, 1.0 x 10^13 GC/kg, and 2.0 x 10^13 GC/kg. A protocol amendment for stage 1 has been approved that removes the use of placebo from this stage of the study. In stage 2, a new cohort of patients will be randomized 2:1 to receive the selected dose of UX701 or placebo. The primary safety and efficacy analyses will be conducted at Week 52 of stage 2. The primary efficacy endpoints are change in 24-hour urinary copper concentration and percent reduction in standard of care medication by Week 52. After the initial 52-week study period, we expect that all patients will receive long term follow up in stage 3.

Completion of Stage 1 enrollment is expected in mid-2023 with data on safety and potentially initial signs of clinical activity expected in early 2024.

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

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

UX053 is an mRNA product candidate designed for the treatment of patients with GSDIII, a disease caused by a glycogen debranching enzyme, or AGL, deficiency that results in glycogen accumulation in the liver and muscle. UX053 has received Orphan Drug Designation in the U.S. and in the EU.

Dosing in the single ascending dose stage of the Phase 1/2 study of UX053 for the treatment of GSDIII has been completed and we expect to have this data in the first half of 2023. Based on these analyses and other work, we will then review our plans for the next steps in the program.

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

**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 and TIO, it is possible that competitors may produce, develop, and commercialize therapeutics, or utilize other approaches such as gene therapy, to treat XLH and TIO. 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 Dojolvi, LC-FAOD is commonly treated with diet therapy and MCT oil. Dojolvi may compete with this approach. Although we believe that Dojolvi 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 Evkeeza, the current treatments for patients with HoFH involve various lipid-lowering agents to reduce serum LDL and total cholesterol levels. Drug therapies include statins (e.g., Rosuvastatin, Simvastatin, etc.), fenofibrate, ezetimibe (Ezetrol), evolocumab (Repatha), and lomitapide (Juxtapid/Lojuxta). Other than lomitapide, these agents rely on an LDL-receptor based mechanism to reduce cholesterol, which may be absent in HoFH patients, particularly those with LDLR-null mutations. In addition, Arrowhead Pharmaceuticals is developing ARO-ANG3 and Eli Lilly/Dicerna is developing LY3561774, both RNAi-based inhibitors of ANGPTL3 in Phase 2 studies across various indications including HoFH.

With respect to DTX401, there are currently no pharmacologic treatments for patients with GSDIa. We are aware of an mRNA therapy, mRNA-3745, in Phase 1 for GSDIa by Moderna.

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 by Acer Therapeutics, was approved in December 2022. 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, Arcturus Therapeutics is developing ARCT-810, a messenger RNA therapy, in Phase 2 for OTC deficiency.

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 and clinical development for Angelman syndrome, including programs from Roche and Biogen in collaboration with Ionis in Phase 1 studies, as well as preclinical gene therapy programs. In addition, Neuren Pharmaceuticals is developing NNZ-2591, an IGF-1 analog, in Phase 2 for Angelman syndrome.

With respect to UX701, there are no currently approved treatments that address the underlying cause of Wilson disease. Many patients are on chelator therapies, but these fail to address the mutated ATP7B copper transporter gene. We are aware of another gene therapy, VTX-801, that is in Phase 1 for Wilson disease by Vivet Therapeutics, in collaboration with Pfizer. In addition, Alexion is developing ALXN1840, a copper chelator in Phase 3.

With respect to UX143, there are currently no approved drugs for osteogenesis imperfecta. Most pediatric patients with osteogenesis imperfecta are managed with off-label use of bisphosphonates to increase bone density and reduce frequency of bone fracture. We are aware of another anti-sclerostin antibody, romosozumab, that is in Phase 1 clinical testing by Amgen. In addition, two anti-TGFβ antibodies, fresolimumab and SAR439459, are in Phase 1 clinical testing by Sanofi-Genzyme.

With respect to UX053, there are currently no pharmacologic treatments for patients with GSD III and we are not aware of any programs in clinical development.

With respect to UX111, there are currently no approved pharmacologic treatments for patients with MPS IIIA. Patients receive supportive or symptomatic treatment, but these approaches generally do not prevent functional decline. We are aware of other gene therapies, including LYS-SAF302, in Phase 2/3 for MPSIIIA by Lysogene, and EGT-101, in Phase 1/2 for MPSIIIA by Esteve. In addition, Orchard Therapeutics is developing OTL-201, an ex-vivo gene therapy in Phase 1/2 for MPSIIIA.

**License and Collaboration Agreements**

Our products and some of our current product candidates 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 collaborate on the development and commercialization of Crysvita in the field of orphan diseases in the U.S. and Canada, or the profit-share territory, and in the EU, U.K., 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 share 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. In April 2023, which is the transition date for the profit-share 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 and U.K. 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, with KKC having the right to increasingly participate in the promotion of the products until the transition date of April 2023, which is five years from commercial launch. In September 2022, we entered into an amendment to the collaboration agreement which clarified the scope of increased participation by KKC in support of our commercial activities prior to April 2023 and granted us the right to continue to support KKC in commercial field activities in the U.S. through April 2024, subject to the limitations and conditions set forth in the amendment. As a result, KKC will continue to support our commercial field and marketing efforts through a cost share arrangement through April 2024, subject to the limits and conditions set forth in the amendment. After April 2024, our rights to promote Crysvita in the U.S. will be limited to medical geneticists and we will solely bear our expenses related to the promotion of Crysvita in the profit-share territory. 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, with the exception of Turkey. In Turkey, we have rights to commercialize Crysvita and KKC has the option to assume responsibility for such commercialization efforts, after a certain minimum period. 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 the 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. In July 2022, we sold to OCM LS23 Holdings LP, an investment vehicle for the Ontario Municipal Employees Retirement System, or OMERS, our right to receive 30% of the future royalty payments due to us based on net sales of Crysvita in the U.S. and Canada, subject to a cap, beginning in April 2023. KKC pays us a royalty of up to 10% based on net sales in the European territory. We sold our interest in the European territory royalty to RPI Finance Trust, an affiliate of 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.

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. 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 the license agreement, we are obligated to pay to SLU a low single-digit royalty on net sales of the licensed products in the U.S., Europe, or Japan, subject to certain potential deductions. Our obligation to pay royalties to SLU in these territories continues until the 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 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 expiration of any orphan drug exclusivity in the U.S., Europe, or Japan, at which point our license becomes fully paid.

***Baylor Research Institute***

In September 2012, we entered into a license agreement, which was subsequently amended, with Baylor Research Institute, or BRI, under which we exclusively licensed certain intellectual property related to Dojolvi. The license includes patents, patent applications, know-how, and intellectual property related to the composition and formulation of Dojolvi 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. During the year ended December 31, 2022, the sales milestone triggering a $2.5 million payment was achieved. Going forward, we may make future payments of up to $2.5 million contingent upon attainment of certain development milestones and $5.0 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.

***Regeneron***

In January 2022, we announced a collaboration with Regeneron to commercialize Evkeeza for HoFH outside of the U.S. Evkeeza is approved in the U.S., where it is marketed by Regeneron, and in the EU and U.K. as a first-in-class therapy for use together with diet and other low-density lipoprotein-cholesterol-lowering therapies to treat adults and adolescents aged 12 years and older with HoFH. Pursuant to the terms of the agreement, we received the rights to develop, commercialize and distribute the product for

HoFH in countries outside of the U.S. Upon closing of the transaction in January 2022, we paid Regeneron a $30.0 million upfront payment. We are obligated to pay Regeneron up to $63.0 million in future milestone payments, contingent upon the achievement of certain regulatory and sales milestones. We may share in certain costs for global trials led by Regeneron and also received the right to opt into other potential indications, including a right to negotiate a separate agreement with Regeneron to collaborate on the Regeneron's investigational antibody for the treatment of fibrodysplasia ossificans progressiva, or FOP, which expired in July 2022.

**Clinical Product Candidates**

***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 Healthcare, LLC, or 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, which was subsequently amended, pursuant to which we have an exclusive worldwide license to make, have made, use, import, sell, and offer for sale licensed products to treat Wilson disease and CDKL5 deficiency. 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, as amended, 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.

In March 2020, we entered into a license agreement with REGENX, for an exclusive, sublicensable, worldwide license to REGENX's NAV AAV8 and AAV9 vectors for the development and commercialization of gene therapy treatments for a rare metabolic disorder. In return for these rights, we made an upfront payment and pay or will pay certain annual fees, milestone payments and royalties on any net sales of products incorporating the licensed intellectual property that range from a high single-digit to low double-digit.

***Bayer***

In June 2014, we entered into an agreement with Bayer to research, develop and commercialize AAV gene therapy products for the treatment of hemophilia A, which was amended and restated in June 2019, or the Collaboration and License Agreement for DTX201. Under this agreement, we granted Bayer an exclusive license to develop and commercialize one or more novel gene therapies for hemophilia. In October 2022, the Collaboration and License Agreement for DTX201 with Bayer was terminated and all licensed rights to DTX201 have reverted to us. We also obtained rights to all necessary data and information to further develop DTX201 or another hemophilia A program through a royalty-free, worldwide, sublicensable, perpetual license. We plan to continue development while seeking a collaboration partner for this program.

***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. The agreement expired on December 31, 2021.

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 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 are required to make milestone payments (up to a maximum of $5.0 million per Subfield) if certain development milestones are achieved over time. We will also make milestone payments of up to $25.0 million per approved product, if certain commercial milestones are achieved, and will pay low to mid- single-digit royalties on net sales of each Subfield’s licensed products.

***GeneTx***

In August 2019, we entered into 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. 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.

In July 2022, we exercised our option to acquire GeneTx and entered into a Unit Purchase Agreement, or the Purchase Agreement, pursuant to which we purchased all the outstanding units of GeneTx. In accordance with the terms of the Purchase Agreement, we exercised our option to acquire GeneTx Biotherapeutics LLC (GeneTx) for an option exercise price of $75.0 million, in addition to outstanding cash and adjustments for working capital, for a total purchase consideration of $91.2 million. We are obligated to make future payments of up to $190.0 million upon the achievement of certain milestones, including up to $30.0 million in milestone payments upon achievement of the earlier of initiation of a Phase 3 clinical study or product approvals in Canada and the U.K., up to $85.0 million in additional regulatory approval milestones for the achievement of U.S. and EU product approvals, and up to $75.0 million in commercial milestone payments based on annual worldwide net product sales. In addition, we are obligated to pay tiered mid- to high single-digit percentage royalties based on licensed product annual net sales. If we receive and resell an FDA priority review voucher, or PRV, in connection with a new drug application approval, GeneTx is entitled to receive a portion of proceeds from the sale of the PRV or a cash payment from us, if we choose to retain the PRV.

***Mereo***

In December 2020, we entered into a License and Collaboration Agreement with Mereo to collaborate on the development of setrusumab. Under the terms of the agreement, we will lead future global development of setrusumab in both pediatric and adult patients with OI and were granted an exclusive license to develop and commercialize setrusumab in the U.S., Turkey, and the rest of the world, excluding the European Economic Area, United Kingdom, and Switzerland, or the Mereo Territory, where Mereo retains commercial rights. Each party will be responsible for post-marketing commitments and commercial supply in their respective territories.

Upon the closing of the transactions under the License and Collaboration Agreement with Mereo in January 2021, we made a payment of $50.0 million to Mereo and will be required to make payments of up to $254.0 million upon the achievement of certain clinical, regulatory, and commercial milestones. We will pay for all global development costs as well as tiered double-digit percentage royalties to Mereo on net sales in the U.S., Turkey, and the rest of the world, and Mereo will pay us a fixed double-digit percentage royalty on net sales in the Mereo Territory.

***Abeona***

In May 2022, we announced an exclusive License Agreement with Abeona for an AAV gene therapy for the treatment of MPS IIIA, or UX111. Under the terms of the agreement, we assumed responsibility for the UX111 program and in return, we are obligated to pay Abeona certain UX111-related prior development costs and other transition costs. Abeona is eligible to receive tiered royalties of up to 10% on net sales and commercial milestone payments of up to $30.0 million following regulatory approval of the product. Additionally, we entered into an Assignment and Assumption Agreement with Abeona to transfer and assign to us the exclusive license agreement between Nationwide Children's Hospital, or NCH, and Abeona for certain rights related to UX111. Under this agreement, NCH is eligible to receive from us up to $1.0 million in development and regulatory milestones as well as royalties in the low single-digits of net sales.

***Arcturus***

In October 2015, we entered into a Research Collaboration and License Agreement with Arcturus Therapeutics Holdings Inc., or Arcturus, to develop mRNA therapeutics for select rare disease targets. As part of the collaboration, we may use Arcturus' LUNAR® nanoparticle delivery platform to develop mRNA therapeutics for the treatment of various rare disease targets, subject to certain exclusions and restrictions.

In June 2019, we announced the expansion of our research and collaboration arrangement with 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 2015 Research Collaboration and License Agreement, or 2015 license agreement, and equity purchase agreement. In connection with the amendment to the 2015 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. In May 2020, we exercised an option to purchase an additional 600,000 shares of Arcturus' common stock at $16.00 per share. During the years ended December 31, 2022 and 2021, we sold 500,000 shares and 1,700,000 shares of Arcturus common stock, respectively, at a weighted-average price of $20.39 and $47.44, respectively. As of December 31, 2022, we held no shares of Arcturus common stock.

On a product-by-product basis, we are obligated to make development and regulatory milestone payments of up to $24.5 million, and commercial milestone payments of up to $45.0 million if certain milestones are achieved. We are also obligated to pay Arcturus royalties on any net sales of products incorporating the licensed intellectual property that range from a mid- single-digit to low double-digit percentage.

**Preclinical Pipeline**

***Solid Biosciences Inc.***

In October 2020, we entered into a strategic Collaboration and License Agreement with Solid Biosciences Inc., or Solid, and received an exclusive license for any pharmaceutical product that expresses Solid's proprietary microdystrophin construct from AAV8 and variants thereof in clade E for use in the treatment of Duchenne muscular dystrophy and other diseases resulting from lack of functional dystrophin, including Becker muscular dystrophy. We are collaborating to develop products that combine Solid's differentiated microdystrophin construct, our Pinnacle PCL™ producer cell line platform, or Pinnacle PCL Platform, manufacturing platform, and our AAV8 variants. Solid may provide some development support and was granted an exclusive option to co-invest in products we develop for profit-share participation in certain territories. We also entered into a Stock Purchase Agreement with Solid in October 2020 pursuant to which we purchased 7,825,797 shares of Solid's common stock for an aggregate price of $40.0 million. In October 2022, Solid announced a 1 for 15 reverse stock split. After the split, we hold 521,719 shares in Solid.

**Platform Technology Transfer**

***Daiichi***

In March 2020, we entered into a License and Technology Access Agreement, or the License Agreement with Daiichi Sankyo Co., Ltd., or Daiichi Sankyo, pursuant to which, we granted Daiichi Sankyo a non-exclusive license to intellectual property, including know-how and patent applications, with respect to our Pinnacle PCL Platform and HEK293 transient transfection manufacturing technology platforms for AAV-based gene therapy products. We retained the exclusive right to use the manufacturing technology for our current target indications and additional indications identified now and in the future. We are providing certain technical assistance and technology transfer services during the technology transfer period of three years to enable Daiichi Sankyo to use the technologies for its internal gene therapy programs. Daiichi Sankyo has an option to extend the technology transfer period including know-how improvements by two additional one-year periods by paying a fixed amount for each additional year. Daiichi Sankyo will be responsible for the manufacturing, development, and commercialization of their products manufactured with the licensed technology; however, we have the option to co-develop and co-commercialize rare disease products at the IND stage. We may also provide strategic consultation to Daiichi Sankyo on the development of both AAV-based gene therapy products and other products for rare diseases.

Under the terms of the License Agreement, Daiichi Sankyo made an upfront payment of $125.0 million and during the fourth quarter of 2021, made an additional payment of $25.0 million upon achievement of the milestones related to the technology transfer of the Pinnacle PCL and HEK293 platforms. Daiichi Sankyo reimbursed us for all costs associated with the transfer of the manufacturing technology and will also pay us a single-digit royalties on net sales of products manufactured with the technology platforms.

In March 2020, we also entered into a Stock Purchase Agreement with Daiichi Sankyo, pursuant to which Daiichi Sankyo purchased 1,243,913 shares of our common stock in exchange for $75.0 million in cash. Daiichi Sankyo is subject to a three-year standstill and restrictions on sale of the shares (subject to customary exceptions or release).

In June 2020, we executed a subsequent license agreement, or the Sublicense Agreement, with Daiichi Sankyo for transfer of certain technology in consideration for a payment of $8.0 million and annual maintenance fees, milestone payments, and royalties on any net sales of products incorporating the licensed intellectual property.

**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 our products, product candidates, processes, 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 U.S. and internationally for our products, product candidates, and processes. Our policy is to patent or in-license the technologies, inventions, and improvements that we consider important to the development of our business. In addition to patent protection, we rely on trade secrets, know-how, and continuing innovation to develop and maintain our competitive position.

We also use other means to protect our products and product candidates, 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 U.S., 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 — Biosimilars and Exclusivity,” “Government Regulation—U.S. Government Regulation — Abbreviated New Drug Applications for Generic Drugs and New Chemical Entity Exclusivity,” “Government Regulation—U.S. Government Regulation — Patent Term Restoration,” “Government Regulation —EU Regulation — Orphan Designation and Exclusivity,” and “Government Regulation—EU Regulation — New Chemical Entity Exclusivity” below for additional information.

We seek regulatory approval for our products and 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. We also 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 products, product candidates, or processes. For more information, please see “Item I.A. Risk Factors Risks Related to Our Intellectual Property.”

As of December 31, 2022, we own, jointly own, or have exclusive rights to more than 225 issued and in-force patents (not including individually validated national patents in European Patent Convention member countries) that cover one or more of our products or product candidates, methods of their use, or methods of their manufacture, including more than 45 in-force patents issued by the U.S. Patent and Trademark Office, or the USPTO. Furthermore, as of December 31, 2022, we own, jointly own, or have exclusive rights to more than 375 pending patent applications, including more than 50 pending U.S. applications.

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, or 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, a Supplementary Protection Certificate, or SPC, may be available to extend the term of certain European patents covering our products; this requires application for an SPC in individual European Patent Convention, or EPC, member countries following product approval. 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. In the U.S., 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 and our clinical-stage product candidates as of December 31, 2022 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, TIO, and various other hypophosphatemic conditions. Pursuant to this license, we have rights to five issued U.S. patents, as well as issued patents and patent applications in other jurisdictions. The U.S. patents expire between 2028 and 2035. In addition to the foregoing patent protections, Crysvita is protected in the U.S. by regulatory exclusivity until 2030 and by orphan drug exclusivity for treating XLH and TIO until 2025 and 2027, respectively.

*Mepsevii (Vestronidase Alfa) Exclusivity*

We own four issued U.S. patents and the corresponding issued foreign patents covering Mepsevii and its use in the treatment of lysosomal storage disorders such as MPS VII. These patents expire in 2035. Mepsevii is also protected in the U.S. by regulatory exclusivity until 2029 and by orphan drug exclusivity for treating MPS VII until 2024.

*Dojolvi (Triheptanoin) Exclusivity*

We have an exclusive license from BRI to patents and patent applications relating to Dojolvi and its use for the treatment of FAOD. The in-licensed BRI patent portfolio includes issued patents in the U.S and Mexico that expire in 2025 and cover Dojolvi, as well as an issued patent in Canada that expires in 2025 and covers the use of Dojolvi for the treatment of FAOD. In the U.S., we have applied to extend the term of a BRI patent covering Dojolvi from 2025 to 2029. Beyond these BRI patents and patent applications, we own a pending U.S. patent application, corresponding foreign patent applications, and issued patents in Australia, Israel, Korea, Malaysia, and Taiwan relating to our pharmaceutical-grade Dojolvi composition; these owned patents and any additional patents issuing from these owned applications are expected to expire in 2034. Dojolvi is also protected in the U.S. by regulatory exclusivity until 2025 and orphan drug exclusivity for treating FAOD until 2027.

*Evkeeza (Evinacumab) Exclusivity*

We have an exclusive license from Regeneron to certain Regeneron patents for the development and commercialization of Evkeeza outside of the U.S. for the treatment of HoFH and other hyperlipidemia/hypercholesterolemia indications. The in-licensed Regeneron patent portfolio includes a patent family containing several issued foreign patents that expire in 2032 and cover the Evkeeza antibody; Regeneron has filed supplementary protection certificates to extend the rights associated with the European patent within this family until 2036 in certain countries. The in-licensed Regeneron patent portfolio contains five other patent families, one of which includes several pending patent applications directed to a stabilized pharmaceutical formulation comprising Evkeeza; we expect any patents emanating from this patent family to expire in 2040. In addition to the foregoing patent protections, Evkeeza is protected in Europe by data exclusivity until 2029 and marketing exclusivity until 2031.

*DTX401 (Pariglasgene Brecaparvovec) Exclusivity*

We have two in-licenses to patents and patent applications covering elements of our DTX401 product candidate. First, we have in-licensed an issued U.S. patent owned by the University of Pennsylvania, or UPENN, and sublicensed to us by REGENX relating to the AAV8 capsid used in DTX401 that expires in 2024. Second, we have a non-exclusive license from the National Institutes of Health, or NIH, to an issued U.S. patent expiring in 2034 (not accounting for any available PTE) and corresponding foreign patents covering a recombinant nucleic acid construct used in DTX401 that includes a codon-optimized version of the G6Pase gene.

*DTX301 (Avalotcagene Ontaparvovec) Exclusivity*

We have a license to two patent families covering elements of our DTX301 product candidate. These patent families are owned by UPENN and sublicensed to us by REGENX. The in-licensed UPENN patent portfolio includes an issued U.S. patent relating to the AAV8 capsid used in DTX301 that expires in 2024, as well as two issued U.S. patents expiring in 2035 (not accounting for any available PTE) and corresponding foreign patents and patent applications covering the codon-optimized version of the OTC gene used in DTX301.

*UX143 (Setrusumab) Exclusivity*

We have in-licensed rights from Mereo to patents and patent applications relating to setrusumab and its use for the treatment of OI. Pursuant to our license from Mereo, we have exclusive rights outside of Europe to a Mereo patent family that includes three issued U.S. patents and corresponding issued foreign patents that relate to the setrusumab antibody, nucleic acids encoding setrusumab, processes for producing setrusumab, and setrusumab's use as a medicament. Patents emanating from this patent family expire in 2028 (not accounting for any available PTE). We also have exclusive rights outside of Europe to two additional Mereo patent families, including an issued U.S. patent expiring in 2037 (not accounting for any available PTE), relating to methods of using anti-sclerostin antibodies including setrusumab for the treatment of OI. Beyond these Mereo patents and patent applications, we jointly own with Mereo a patent family relating to dosing regimens for the use of anti-sclerostin antibodies including setrusumab in the treatment of OI; we expect any patents emanating from this patent family to expire in 2042 (not accounting for any available PTE).

*DTX201 (Peboctocogene Camaparvovec) Exclusivity*

We have a license to two patent families covering elements of our DTX201 product candidate. These patent families are owned by UPENN and sublicensed to us by REGENX. The in-licensed UPENN patent portfolio includes three issued U.S. patents and corresponding foreign patents relating to the AAVhu37 capsid used in DTX201 that expire in 2024, as well as an issued U.S. patent expiring in 2037 (not accounting for any available PTE) and corresponding foreign patents and patent applications covering the codon-optimized version of the Factor VIII gene used in DTX201.

*UX111 Exclusivity*

We have an exclusive license from Nationwide Children's Hospital, or NCH, to a pending U.S. patent application covering a method of treating MPS IIIA by intravenously administering a recombinant AAV9 vector comprising a U1a promoter and a polynucleotide sequence encoding N-sulfoglucosamine sulfohydrolase, or SGSH; we expect any patent emanating from this application to expire in 2032 (not accounting for any available PTE).

*GTX-102 Exclusivity*

We have an exclusive license from Texas A&M University, or TAMU, to a patent family filed in the U.S. and several foreign jurisdictions relating to UBE3A antisense oligonucleotides including GTX-102 and their use for the treatment of Angelman syndrome,

or AS. The in-licensed TAMU patent family includes an issued U.S. patent expiring in 2038 (not accounting for any available PTE) that covers a method of using GTX-102 for the treatment of AS.

*UX701 Exclusivity*

We have two licenses to patents and patent applications covering elements of our UX701 product candidate. First, we have in-licensed patents owned by UPENN and sublicensed to us by REGENX relating to the AAV9 capsid used in UX701 that expire between 2024 and 2026 in the U.S., and in 2024 in foreign countries. Second, we have an exclusive license from UPENN to a patent family filed in the U.S. and several foreign jurisdictions relating to AAV vectors containing certain regulatory and coding sequences packaged in UX701; this patent family includes an issued U.S. patent expiring in 2039 (not accounting for any available PTE). Beyond these in-licenses, we own a patent family covering AAV vectors expressing a novel truncated version of the ATP7B protein produced by UX701; we expect any patents emanating from this patent family to expire in 2040 (not accounting for any available PTE).

*UX053 Exclusivity*

We have a license from Arcturus to four issued U.S. patents expiring between 2034 and 2038 (not accounting for any available PTE), and corresponding foreign patents and applications, that cover the cationic lipid used in our UX053 product candidate. Beyond these Arcturus patents and patent applications, we own a patent family filed in the U.S. and several foreign jurisdictions covering the codon-optimized version of the human AGL mRNA contained in UX053; this patent family includes an issued U.S. patent expiring in 2039 (not accounting for any available PTE).

***Trademarks***

We own registered trademarks covering the Ultragenyx word mark in the U.S. and multiple other jurisdictions. In addition, we have a pending trademark application in the U.S. covering a stylized design of our Ultragenyx logo. We also own registered trademarks in the U.S. and other territories relating to our Mepsevii and Dojolvi brand names for vestronidase alfa and triheptanoin, respectively. We additionally have licenses from KKC and Regeneron to registered trademarks covering the Crysvita and Evkeeza brand names, respectively, in territories where we have rights to commercialize these products.

***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 and nucleic acid technologies. The use of contracted manufacturing and reliance on collaboration partners has historically minimized 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 are building our own GMP gene therapy manufacturing plant to seek to mitigate potential program timeline delays, control manufacturing costs and reduce manufacturing lead times. 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 is 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 and such breach remains uncured for a specified period following receipt by the breaching party of written notice of such breach. We can also terminate the agreement 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 transferred the fill and finish activities for the manufacture of Mepsevii Drug Product to a new site, BSP Pharmaceuticals S.p.A., or BSP, located in Latina, Italy as the Rentschler manufacturing site in Laupheim, Germany was discontinued. The site change was approved by relevant global authorities, including the FDA, on May 5, 2022. Sufficient inventory levels were maintained during the transfer of the fill and finish activities for Mepsevii to BSP.

*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.

*Dojolvi*

The pharmaceutical-grade drug substance for Dojolvi 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. The drug product for Dojolvi is manufactured by Aenova Haupt Pharma Wolfratshausen GmbH, or Haupt Pharma, pursuant to a Master Services Agreement, for the non-exclusive manufacture and supply of product. The agreement was executed in April 2019 with an initial three-year term and automatically renews at the end of the current term for an indefinite period unless we provide written notice of termination to Haupt Pharma no later than 60 days prior to the expiration of the initial term. After the initial term, either party may terminate the agreement without cause with at least 12 months' notice. Additionally, if a party materially breaches certain obligations under the agreement and does not cure such breach within 30 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. Either party may also terminate the agreement with immediate effect if the other party breaches certain specified obligations as set forth in the agreement.

*Evkeeza*

On January 7, 2022, we announced a license and collaboration agreement with Regeneron for us to clinically develop, commercialize and distribute Evkeeza in countries outside of the U.S. Evkeeza is a fully human monoclonal antibody that binds to and blocks the function of angiopoietin-like 3, or ANGPTL3, a protein that plays a key role in lipid metabolism.

The Evkeeza drug substance is manufactured by Regeneron at their manufacturing facility in Rensselaer, New York and the drug product is manufactured by Baxter Pharmaceutical Solutions, LLC. at their manufacturing facility in Bloomington, Indiana. Release testing of the drug product is performed by Regeneron and third-party suppliers.

We utilize third-party suppliers to perform packaging, labelling, distribution, and testing as needed for Evkeeza.

**Product Candidates**

The drug substances and drug products for our product candidates are manufactured using our network of GMP contract manufacturing organizations, or CMOs, which are carefully selected and actively managed for high quality, reliable clinical supply. The CMOs are located in Western Europe or North America.

**Commercialization and Product Support**

We have built our own commercial organizations in North America, Europe, Latin America and Japan to effectively support the commercialization of our products and product candidates, if approved. Our intention is to expand our product portfolio and its geographic accessibility through the continued development of our proprietary pipeline or through strategic partnerships. We may elect to utilize strategic partners, distributors, or contract management organizations to assist in the commercialization of our products in certain geographies. 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 patient support services, distribution, and market access. One challenge, unique to commercializing therapies for rare diseases, is the difficulty in identifying eligible patients due to the very small and sometimes heterogeneous patient populations along with often undefined clinical or genetic tests to confirm diagnosis. Our commercial and medical affairs teams focus on maximizing patient identification for both clinical development and commercialization purposes in rare diseases.

Additional capabilities important to the rare disease marketplace in the U.S. include the management of key stakeholders such as managed care organizations, specialty pharmacies, and government payers. In many countries outside the U.S. single national payers are critical to providing reimbursement access. 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 support commercial and medical affairs organizations as well as other capabilities across North America, Europe, Latin America, and Japan to meet the scientific educational needs of the healthcare providers and patients in the rare disease community, focusing on providing accurate disease state information 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 liaisons, 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 U.S. (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 U.S. 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 that has a significant impact on our capital expenditures and results of operations.

***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 investigational new drug application, or 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 U.S., 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 U.S. 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 U.S. 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 and the U.S. Department of Agriculture's Animal Welfare Act;
- 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 that generally follow the three- to four-phase design described above 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 if it finds the application has adequate support for commercial marketing. 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, or 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. The FDA may also issue a Complete Response Letter, which indicates that the review cycle of the application is complete but 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. If the conditions set forth in the Complete Response Letter are met, the FDA may approve the product for marketing.

*Expedited Review and Accelerated Approval Programs*

A sponsor may seek approval of its product candidate under programs designed to accelerate the 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 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 a breakthrough therapy, the 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, or 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.

The 2023 Consolidated Appropriations Act strengthens the FDA's authority to require and regulate post-approval studies of accelerated approval drugs and to expedite the rescission of accelerated approval based on the post-approval studies.

*Orphan Designation and Exclusivity*

Under the Orphan Drug Act, 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 U.S., or if it affects more than 200,000 individuals in the U.S. 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 U.S.

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 U.S., 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.

There is some uncertainty with respect to the FDA's interpretation of the scope of orphan drug exclusivity. Historically, exclusivity was specific to the orphan indication for which the drug was approved. As a result, the scope of exclusivity was interpreted as preventing approval of a competing product. However, in 2021, the federal court in Catalyst Pharmaceuticals, Inc. v. Becerra, suggested that orphan drug exclusivity covers the full scope of the orphan-designated "disease or condition" regardless of whether a drug obtained approval for a narrower use.

*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. 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 U.S. 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.

The Inflation Reduction Act of 2022, or the IRA, is intended to foster generic and biosimilar competition and to lower drug and biologic costs. The IRA provides the Centers for Medicare & Medicaid Services, or CMS, with significant new authorities. CMS will be able to directly negotiate prescription drug prices and to cap out-of-pocket costs. Each year, CMS will select and negotiate a preset number of high-spend drugs and biologics covered under Medicare Parts B and D that lack generic or biosimilar competition. Price negotiations begin in 2023. Taking effect in 2023, the IRA provides a new "inflation rebate" that covers Medicare patients and is intended to counter certain price increases in prescription drugs. The inflation rebate requires drug manufacturers to pay a rebate to the federal government if the price for a drug or biologic under Medicare Parts B or D increases faster than the rate of inflation. To support biosimilar competition, qualifying biosimilars may receive a Medicare Part B payment increase for a period of five years, beginning in October 2022. Separately, if a biologic drug for which no biosimilar exists delays a biosimilar's market entry beyond two years, CMS will be authorized to subject the biologics manufacturer to price negotiations intended to ensure fair competition. Notwithstanding these provisions, the IRA's impact on competition and commercialization remains largely uncertain.

*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 and in Iceland, Norway and Liechtenstein, together the European Economic Area or EEA, after completion of all required clinical testing, pharmaceutical products may only be placed on the market after obtaining a Marketing Authorization, or MA. To obtain a MA, 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 U.S., with the exception of, among other things, country-specific document requirements.

*Authorization Procedures*

Medicines can be authorized by using, among other things, a centralized or decentralized procedure. The centralized authorization procedure results in a single marketing authorization issued by the European Commission, or EC, following the scientific assessment of the application by the European Medicines Agency, or EMA, that is valid across the EEA. The centralized procedure is compulsory for specific medicinal products, including medicines developed by means of certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products, or ATMPs, and medicinal products with a new active substance indicated for the treatment of certain diseases (for instance, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases). 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).

All new MAAs must include a Risk Management Plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available. We need to submit an updated RMP: (i) at the request of EMA or a national competent authority, or (ii) whenever the risk-management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit-risk profile or as a result of an important pharmacovigilance or risk-minimization milestone being reached. The regulatory authorities may also impose specific obligations as a condition of the MA. RMPs and Periodic Safety Update Reports, or PSURs, are routinely available to third parties requesting access, subject to limited redactions.

Special rules apply in part for ATMPs. ATMPs comprise gene therapy products, somatic cell therapy products and tissue engineered products, which are genes, cells or tissues that have undergone substantial manipulation and that are administered to human beings in order to cure, diagnose or prevent diseases or regenerate, repair or replace a human tissue. Pursuant to the ATMP Regulation, the Committee on Advanced Therapies, or CAT, is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CHMP and CAT are also responsible for providing guidelines on ATMPs. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs. The manufacturing and control information that should be submitted in a MAA; and post-approval measures required to monitor patients and evaluate the long- term efficacy and potential adverse reactions of ATMPs. Although such guidelines are not legally binding, compliance with them is often necessary to gain and maintain approval for product candidates. In addition to the mandatory RMP, the holder of a MA for an ATMP must put in place and maintain a system to ensure that each individual product and its starting and raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the relevant healthcare institution where the product is used.

A Pediatric Investigation Plan, or PIP, and/or a request for waiver (for example, because the relevant disease or condition occurs only in adults) or deferral (for example, until enough information to demonstrate its effectiveness and safety in adults is available), 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 Committee for Medicinal Products for Human Use, or CHMP, established at the EMA, is responsible for conducting the initial assessment of a drug. In principle, the maximum timeframe for the evaluation of an MAA by the CHMP is 210 days from receipt of a valid MAA. However, this timeline excludes clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP, so the overall process typically takes a year or more. A favorable opinion on the application by the CHMP will typically result in the granting of the marketing authorization within 67 days of receipt of the opinion. 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, and upon request by the applicant, the CHMP's evaluation time frame is reduced to 150 days, excluding time taken by an applicant to respond to questions.

*MA Validity Period*

MAs have an initial duration of five years. After five years, the authorization may subsequently be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with only one additional five-year renewal. Applications for renewal must be made to the EMA at least nine months before the five-year period expires.

*Conduct of Clinical Trials*

Clinical trials are studies intended to discover or verify the effects of one or more investigational medicines. The regulation of clinical trials aims to promote the protection of the rights, safety and well-being of trial participants and the credibility of the results of clinical trials. Regardless of where they are conducted, all clinical trials included in applications for marketing authorization for human medicines in the EU or EEA must have been carried out in accordance with EU regulations (such as, among others, the Clinical Trials Regulation (Regulation (EU) No 536/2014) and the Clinical Trials Directive (EC) No 2001/20/EC). This means that clinical trials conducted in the EU or EEA have to comply with EU clinical trial legislation and that clinical trials conducted outside the EU or EEA have to comply with ethical principles equivalent to those set out in the EEA, including adhering to international good clinical practice and the Declaration of Helsinki.

*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. A conditional MA 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 MAs can be granted for medicinal products where, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, a number of criteria are fulfilled: (i) the benefit/risk balance of the product is positive, (ii) it is likely that the applicant will be in a position to provide the comprehensive clinical data, (iii) unmet medical needs will be fulfilled by the grant of the MA and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. Conditional MAs are valid for only one year and must be reviewed annually subject to certain specific obligations.

*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. PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

*Orphan Designation and Exclusivity*

As in the U.S., 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. The applicant will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted, and sponsors must submit an annual report to EMA summarizing the status of development of the medicine. 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, or NCEs, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon the product's first MA in the EU 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. Products may not be granted data exclusivity since there is no guarantee that a product will be considered by the EU's regulatory authorities to include an NCE. Even if a compound is considered to be a NCE and the MA applicant is able to gain the prescribed period of data exclusivity, another company could market a version of the medicinal product if such company can complete a full MAA with its own complete database of pharmaceutical tests, preclinical studies and clinical trials and obtain MA of its product.

***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 U.S. 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, including volume-based arrangements, caps and reference pricing mechanisms. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

***Other Healthcare, Privacy, and Cybersecurity Laws and Compliance Requirements***

We are subject to various laws targeting, among other things, fraud and abuse in the healthcare industry, and privacy and protection of personal information, including health information. 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, or GDPR, which applies to processing of personal data in the context of the activities of an establishment in the EEA, and to processing related to the offering of goods or services to individuals who are in the EEA, or the monitoring of individuals who are in the EEA, and imposes requirements and limitations relating to the processing, storage, purpose of collection, accuracy, security, sharing and transfer of personal data outside the EEA, in particular with respect to special categories of personal data like health 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 various healthcare professionals and teaching hospitals; and
- state and foreign law equivalents, or similar, 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, including comprehensive privacy and security laws in California, and others taking effect in 2023.

***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 or in EU member states, 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. Complying with these requirements may have a significant impact on our capital expenditures and results of operations.

**Customers**

Our customers include collaboration partners, drug wholesalers, and retail pharmacy distributors. For the year ended December 31, 2022, more than half of our total revenues were generated under our collaboration agreement with KKC.

**Human Capital**

*General Information*

As of December 31, 2022, we had 1,311 total employees, of which 705 are in research and development and 606 are in sales, general, and administrative. Further, 1,155 are based in the U.S., including at our facilities in Novato, California, Brisbane, California, Cambridge, Massachusetts, and Woburn, Massachusetts, and 156 are based at our international locations. The majority of new employees hired during the year ended December 31, 2022 were to support and extend our clinical and preclinical pipeline as well as our commercialization activities, with hires in commercial, clinical development and operations, research, manufacturing, and general and administrative functions. We believe our relationship with our employees to be generally good. We have not experienced any material employment-related issues or interruptions of services due to labor disagreements and are not a party to any collective bargaining agreements.

We expect to continue to add employees in 2023 with a focus on expanding our in-house manufacturing capacity in connection with completing construction of our gene therapy manufacturing facility, increasing expertise and bandwidth in clinical and preclinical research and development and commercialization activities and expanding our geographic reach in connection with the global launches of our approved products. We continually evaluate our business need and opportunity and balances in-house expertise and capacity with outsourced expertise and capacity. Currently, we outsource substantial clinical trial work to clinical research organizations and certain drug manufacturing to contract manufacturers.

*Workforce Safety and Employee Wellbeing*

We maintain a safety culture grounded on the premise of eliminating workplace incidents, risks and hazards. The COVID-19 pandemic provided an opportunity for us to demonstrate our commitment to the health and wellbeing of our employees. Effective as of January 3, 2022, we have required full vaccination against COVID-19 as a condition of employment at the company for almost all roles based in the U.S., with limited exceptions. We have adopted a flexible, hybrid working arrangement for employees, which allows some of our employees to work remotely during certain days of the week. To support our employees, we have provided collaboration tools and resources for employees working remotely, including training and toolkits to help leaders effectively lead and manage remote teams, expanded employees assistance and mindfulness programs to help employees and their families manage anxiety, stress, and overall wellbeing and increased investment in resources focused on inclusion and belonging.

*Employee Retention and Engagement*

The biotechnology industry is an extremely competitive labor market and we believe our company’s success depends on our ability to attract, develop, and retain key personnel. We invest in the growth and development of our employees through various training and development programs that build and strengthen employees’ leadership and professional skills, including leadership development programs for new leaders, as well as a mentoring program. We also have a talent management framework and processes in place that includes regularly conducted activities such as performance management, succession, and workforce planning in order to support our employees in their growth and development and to provide learning opportunities. We encourage all employees to have an individual development plan to identify focus areas for learning and growth.

To continually assess and improve our employee retention and engagement, we conduct an engagement survey approximately every 18 months, with "pulse" surveys in between, the results of which are discussed with our board of directors, at all hands employee meetings and in individual functions. We take actions to address areas of employment concern and follow-up routinely to share with employees what we are doing.

*Inclusion and Diversity*

We strive toward having a diverse organization and are committed to equality, inclusion, and workplace diversity. As of December 31, 2022, of the nine members of our board of directors, three directors were women, three directors self-identified as racially or ethnically diverse, and one director self-identified as LGBTQ+. As of December 31, 2022, women represented approximately 57% of our global workforce and approximately 45% of our leadership positions at the Vice President level or above. As of December 31, 2022, approximately 45% of our U.S. workforce that self-reported identified as racially or ethnically diverse. We have included questions in our engagement survey to measure employee perception of our inclusive culture, with the results from such survey on inclusion and diversity included in our corporate goals for fiscal year 2022 and 2023. Our business units review diversity data related to hiring, promotions, and retention on an ongoing basis. We have also established an Inclusion and Diversity Action Team, or I&D Action Team, comprised of employee representatives throughout our company. Amongst other initiatives, our I&D Action Team engages in continual discussions across the various business functions to identify potential actions to address areas of improvement and is focused on building accountability across the organization to help us meet our diversity objectives. In our efforts to promote diversity and inclusion, we have established or supported several internal employee resource groups (ERGs), including UltraProud and X2 Women in Biotech. In 2022, we hosted an ERG Summit with the objective of bringing together leaders and members of these groups to share their experiences, learn from each other, collaborate on solutions, and network in order to make a greater impact on the company, its employees, and the wider community.

*Benefits and Compensation*

We are dedicated to fostering a workplace environment that keeps our employees inspired, including providing a comprehensive benefits program that supports the health care, family, and financial needs of our employees. All of our full-time employees are eligible for cash bonuses and equity awards in addition to other benefits including comprehensive health insurance, life and disability insurance, 401(k) matching, paid time off for volunteering, wellness programs, and tuition reimbursement. We benchmark and tie compensation to market data as well as to an employee's experience, function and performance. We regularly review our workforce compensation practices and strive for equity.

**General Information**

Our Internet website address is *www.ultragenyx.com.* No portion of our website, or any other website that may be referenced, 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 the SEC. In particular, please read our definitive proxy statements, our Annual Reports on Form 10-K, 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 annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those 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 material 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. The risks and uncertainties described below are not the only ones we face. Additional risk and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. 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. Our company's business, financial condition and operating results can be affected by a number of factors, whether currently known or unknown, including but not limited to those described below, any one or more of which could, directly or indirectly, cause our actual financial condition and operating results to vary materially from past, or from anticipated future, financial condition and operating results. Any of these factors, in whole or in part, could materially and adversely affect our business, prospects, financial condition, operating results and stock price.*

*Because of the following factors, as well as other factors affecting our financial condition and operating results, past financial performance should not be considered to be a reliable indicator of future performance, and investors should not use historical trends to anticipate results or trends in future periods.*

**Risk Factor Summary**

- We have a history of operating losses and anticipate that we will continue to incur losses for the foreseeable future.
- We have limited experience in generating revenue from product sales.
- We expect to need to raise additional capital to fund our activities.
- Clinical drug development is a lengthy, complex, and expensive process with uncertain outcomes.
- Adverse effects if we do not achieve our projected development goals in the time frames we announce and expect.
- We may experience difficulty in enrolling patients.
- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy and inherently unpredictable.
- Fast Track Product, Breakthrough Therapy, Priority Review or RMAT Designations by the FDA, and analogous designations by the EMA, for our product candidates may not lead to faster development or approval.
- Our product candidates may cause undesirable or serious side effects.
- We face a multitude of manufacturing risks, particularly with respect to our gene therapy and mRNA product candidates.
- Our products remain subject to regulatory scrutiny even if we obtain regulatory approval.
- Product liability lawsuits against us could cause us to incur substantial liabilities.
- We may not realize the full commercial potential of our product candidates if we are unable to source and develop effective biomarkers.
- We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us.
- 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.
- We rely on third parties to manufacture our products and product candidates.
- The loss of, or failure to supply by, any of any of our single-source suppliers for our drug substance and drug product could adversely affect our business.
- The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably.
- Our revenue may be adversely affected if the market opportunities for our products and product candidates are smaller than expected.
- Our competitors may develop therapies that are similar, more advanced, or more effective than ours.

- We may not successfully manage expansion of our company, including building an integrated commercial organization.
- Our exclusive rights to promote Crysvita in the U.S. and Canada will transition back to KKC.
- Commercial success of our products depends on the degree of market acceptance.
- We face uncertainty related to insurance coverage and reimbursement status of our newly approved products.
- If we, or our third-party partners, are unable to maintain effective proprietary rights for our products or product candidates, we may not be able to compete effectively.
- Claims of intellectual property infringement may prevent or delay our development and commercialization efforts.
- We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.
- We may face competition from biosimilars of our biologics product and product candidates or from generic versions of our small-molecule product and product candidates, which may result in a material decline in sales of affected products.
- We could lose license rights that are important to our business if we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties.
- We may become involved in lawsuits to protect or enforce our patents or the patents of our licensors, or be subject to claims that challenge the inventorship or ownership of our patents.
- Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.
- We may not be able to protect our intellectual property rights throughout the world.
- We have no experience as a company developing or operating a manufacturing facility.
- Our success depends in part on our ability to retain our President and Chief Executive Officer and other qualified personnel.
- Our revenue may be impacted if we fail to obtain or maintain orphan drug exclusivity for our products.
- Our operating results may be adversely impacted if our intangible assets become impaired.
- We may not be successful in identifying, licensing, developing, or commercializing additional product candidates.
- We may fail to comply with laws and regulations or changes in laws and regulations could adversely affect our business.
- We are exposed to risks related to international expansion of our business outside of the U.S.
- Our business may be adversely affected in the event of computer system failures or security breaches.
- We or our third-party partners may be adversely affected by earthquakes or other serious natural disasters.
- We may incur various costs and expenses and risks related to acquisition of companies or products or strategic transactions.
- The market price of our common stock is highly volatile.
- Future sales and issuances of our common stock could dilute the percentage ownership of our current stockholders and result in a decline in stock price.
- 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 or could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.
- We face general risks related to our ability to maintain effective internal controls over financial reporting, additional tax liabilities related to our operations, our ability to use our net operating loss carryforwards, costs of litigation, stockholder activism and increased scrutiny regarding our ESG practices and disclosures.

**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;
- expand upon or build our own manufacturing-related facilities and capabilities, including construction of 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 have limited experience in generating 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, 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, or any other reasons, we may not generate significant revenue from sales of our products, even if they receive regulatory approval.

***We expect to 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, 2022, our available cash, cash equivalents, and marketable debt securities were $896.7 million. We expect we will 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, such as our GMP gene therapy manufacturing plant;
- 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, 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 can 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, particularly in light of the current macroeconomic conditions, including the general economic slowdown and potential recessionary environment. The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities by us, whether equity or debt, 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 transactions with Royalty Pharma and OMERS or through collaborative partnerships, strategic alliances, and licensing or other arrangements, such as our transaction with Daiichi Sankyo, 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, complex, 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, complex, 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. Our clinical trial activities, including the initiation and completion of such activities and the timing thereof, have been and are expected to continue to be significantly delayed or disrupted by COVID-19. The pandemic has impacted enrollment of patients in certain of our clinical trials and has required us to change the way certain of our clinical trials are conducted. Healthcare resources have been and may continue to be diverted away from the conduct of clinical trials, such as the diversion of hospitals serving as our clinical trial sites, in response to the COVID-19 pandemic and resurgences or mutations of the virus. We have also had difficulties in recruiting clinical site investigators and clinical staff for our studies, and may continue to experience such difficulties. Additionally, 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 or fail 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. Further, we have reported and expect to continue to report preliminary or interim data from our clinical trials. Preliminary or interim data from our clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and/or more patient data become available. Such data may show initial evidence of clinical benefit, but as patients continue to be assessed and more patient data become available, there is a risk that any therapeutic effects are no longer durable in patients and/or decrease over time or cease entirely. As a result, preliminary or interim data should be considered carefully and with caution until the final data are available. 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 devise newly-defined endpoints to be tested in our studies, which can lead to 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 delaying or 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 can 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, or mRNA, DNA, small interfering RNA, or 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, including as a result of hyperinflation;
- 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 time frames 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 timing, type or clarity of data from clinical trials, 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 due to a variety of factors, including the limited number of patients who have the diseases for which our product candidates are being studied and other unforeseen events, such as the COVID-19 pandemic. 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 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 AAV viral vector.

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 is costly and time-consuming, especially since the rare diseases we are studying are commonly underdiagnosed. 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. Additionally, the COVID-19 pandemic has impacted enrollment of patients in certain of our clinical trials for our product candidates as patients have been more reluctant to conduct in-person visits at the sites due to concerns over COVID-19. 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 (such as drug-related side effects), the timeline for and our success in recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed or impaired, 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. 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.

***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 three products that we have developed, 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. Further, as 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 candidates, 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, leading to fewer product approvals. To date, very few gene therapy products have received regulatory approval in the U.S. or Europe. The regulatory framework and oversight over development of gene therapy products has evolved and may continue to evolve in the future. Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within the CBER, the review of gene therapy and related products is consolidated in the Office of Cellular, Tissue and Gene Therapies, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The CBER works closely with the National Institutes of Health, or NIH. The FDA and the NIH have published guidance with respect to the development and submission of gene therapy protocols. For example, in January 2020, the FDA issued final guidance to set forth the framework for the development, review and approval of gene therapies. The final guidance pertains to the development of gene therapies for the treatment of specific disease categories, including rare diseases, and to manufacturing and long-term follow up issues relevant to gene therapy, among other topics. At the same time the FDA issued new draft guidance describing the FDA's approach for determining whether two gene therapy products were the same or different for the purpose of assessing orphan drug exclusivity; the draft guidance was finalized by the FDA in September 2021. Within the European Medicines Agency, or EMA, special rules apply to gene therapy and related products as they are considered advanced therapy medicinal products, or ATMPs. Pursuant to the ATMP Regulation, the Committee on Advanced Therapies, or CAT, is responsible in conjunction with the Committee for Medicinal Products for Human Use, or CHMP, for the evaluation of ATMPs. The CHMP and CAT are also responsible for providing guidelines on ATMPs. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs. The manufacturing and control information that should be submitted in a MAA; and post-approval measures required to monitor patients and evaluate the long-term efficacy and potential adverse reactions of ATMPs. Although such guidelines are not legally binding, compliance with them is often necessary to gain and maintain approval for product candidates. In addition to the mandatory risk-management plan, or RMP, the holder of a marketing authorization for an ATMP must put in place and maintain a system to ensure that each individual product and its starting and raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport, and delivery to the relevant healthcare institution where the product is used.

To obtain regulatory approval in the U.S. 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, as described above in "Item 1. Business – Government Regulation". 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. 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;
- the FDA may be delayed in responding to our applications or submissions due to competing priorities or limited resources, including as a result of the COVID-19 pandemic, lack of FDA funding or personnel;
- failure of our nonclinical or clinical development to comply with an agreed upon Pediatric Investigational Plan, or 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 do 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 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.

***Fast Track, Breakthrough Therapy, Priority Review, or Regenerative Medicine Advanced Therapy, or RMAT, designation by the FDA, or access to the Priority Medicine scheme, or PRIME, by the EMA, for our product candidates, if granted, may not lead to faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.***

As described in "Item 1. Business – Government Regulation", we may seek Fast Track, Breakthrough Therapy designation, RMAT Designation, PRIME scheme access or Priority Review designation for our product candidates if supported by the results of clinical trials. Designation as a Fast Track product, Breakthrough Therapy, RMAT, PRIME, or Priority Review product is within the discretion of the relevant regulatory agency. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a Fast Track product, Breakthrough Therapy, RMAT, PRIME, or Priority Review product, the agency may disagree and instead determine not to make such designation. The receipt of such a designation for a product candidate also may not result in a faster development process, review or approval compared to drugs considered for approval under conventional regulatory procedures and does not assure that the product will ultimately be approved by the regulatory authority. In addition, regarding Fast Track products and Breakthrough Therapies, the FDA may later decide that the products no longer meet the conditions for qualification as either a Fast Track product, RMAT, or a Breakthrough Therapy or, for Priority Review products, decide that period for FDA review or approval will not be shortened. Furthermore, with respect to PRIME designation by the EMA, PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

The FDA Rare Pediatric Disease Priority Review Voucher Program, or PRV Voucher Program, awards Priority Review Vouchers, or PRVs, to sponsors of rare pediatric product applications that meet certain criteria. Under the program, a company that receives an approval for a product for a rare pediatric disease (as determined by the applicable regulations) may qualify for a PRV that can be redeemed to receive Priority Review of a subsequent marketing application for a different product. PRVs may also be sold by the company to third parties. We received PRVs under the PRV Voucher Program in connection with the approval of Mepsevii and Crysvita in 2018 and subsequently sold these two PRVs to third parties for an average amount of $105.3 million for each PRV. The current PRV Voucher Program is scheduled to sunset such that the FDA may only award a PRV for a product application if a company receives the rare pediatric disease designation from the FDA for the product candidate by September 30, 2024, and the FDA will cease awarding PRVs after September 30, 2026. Extension of the current PRV Voucher Program is subject to approval by Congress and it is currently uncertain whether the program will be extended. If our qualifying product candidates are approved by the FDA after the current approval deadlines, we will not be eligible to receive additional PRVs for our product candidates and accordingly, we would be unable to use such PRV for Priority Review for another one of our programs or to sell such PRV, which sale has the potential to generate significant proceeds.

***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. Further, as one of the goals of Phase 1 and/or 2 clinical trials is to identify the highest dose of treatment that can be safely provided to study participants, adverse side effects, including serious adverse effects, have occurred in certain studies as a result of changes to the dosing regimen during such studies and may occur in future studies. 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.

Additionally, notwithstanding our prior or future regulatory approvals for our product candidates, 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.

***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, certain gene therapy trials using AAV8 vectors (although at significantly higher doses than those used in our gene therapy product candidates) and other vectors led to several well-publicized adverse events, including cases of leukemia and death. The risk of cancer or death 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.

***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, malfunctions of internal information technology systems, regulatory inspections, facility contamination, raw material shortages or contamination, natural disasters, geopolitical instability, the COVID-19 pandemic, disruption in utility services, human error or disruptions in the operations of our suppliers. Further, given that cGMP gene therapy, mRNA, DNA and siRNA 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.

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.

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

Our products and any product candidates that are approved in the future remain 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 U.S. and requirements of comparable foreign regulatory authorities, as described above in “Item 1. Business – Government Regulation.”

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, or GMP, regulations. As such, we and our contract manufacturers are 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. Regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our products, product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If we, our collaborators, such as KKC or Regeneron, 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, 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 or withdrawal of product approval. If supply from one approved manufacturer is interrupted due to failure to maintain regulatory compliance, 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 delays in product supply. The regulatory agencies may also require additional studies if a new manufacturer, material, testing method or standard is relied upon for commercial production. Switching manufacturers, materials, test methods or standards may involve substantial costs and may result in a delay in our desired clinical and commercial timelines. Accordingly, we and others with whom we work are required 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. 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.

***Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of our approved products or product candidates.***

We face an inherent risk of product liability exposure related to the testing of our approved products and product candidates in human clinical trials, as well as in connection with commercialization of our current and future products. If we cannot successfully defend ourselves against claims that any of our approved products or product candidates caused injuries, we could incur substantial liabilities. There can be no assurance that our product liability insurance, which provides coverage in the amount of $15.0 million in the aggregate, will be sufficient in light of our current or planned clinical programs. 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.

***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. We can offer no assurances that any current or 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 successfully develop companion diagnostics, we 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 are currently working with a third party to develop companion diagnostics, however, we have little experience in the development and commercialization of diagnostics and may not ultimately be successful in developing and commercializing appropriate diagnostics to pair with any of our product candidates that receive marketing approval. We rely on 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 U.S. as medical devices and require regulatory clearance or approval prior to commercialization. In the U.S., 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 U.S., 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. 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 we cannot control whether or not they devote sufficient time and resources to our on-going nonclinical and clinical programs, except for the limited remedies available to us under our agreements with such third parties. 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, 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. Our efforts to manage our relationships with our vendors and partners can provide 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 certain specified times, in the U.S., Canada, and Turkey, subject to certain rights retained by us. 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 U.S. 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 or commercial use (including as a result of the COVID-19 pandemic), which could result in program delays or 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 our product candidates and we are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit the supply of our product and product candidates.***

As 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 third parties to manufacture our products and product candidates. 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. See "- *Even if we obtain regulatory approval for our product candidates, our products remain subject to regulatory scrutiny"* risk factor above. Further, we depend on our manufacturers to purchase from third-party suppliers the materials necessary to produce our products and product candidates. 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 or mitigate a possible disruption of the manufacture of the materials necessary to produce our products and 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.

Further, manufacturers that produce our products and product candidates may not have experience producing our products and product candidates at commercial levels and may not produce our products and product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization. We have not yet secured manufacturing capabilities for commercial quantities of 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 acceptable manufacturing processes that provide the necessary quantities of our products and product candidates in a compliant and timely manner, 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. For instance, KKC is our sole supplier of commercial quantities of Crysvita. The supply price to us for commercial sales of Crysvita in Latin America and the transfer price for commercial sales of the product in the U.S. and Canada was 35% of net sales through December 31, 2022 and is 30% thereafter, which is higher than the typical cost of sales for companies focused on rare diseases.

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, actual or threatened public health emergencies, 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. 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 have, and may in the future, be required 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 or unwilling 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. For example, the drug substance and drug product for Crysvita and Evkeeza are made, respectively, by KKC pursuant to a license and collaboration agreement and Regeneron pursuant to a supply agreement. The drug substance and drug product for Mepsevii are currently manufactured by Rentschler under a commercial supply and services agreement, accompanying purchase orders, and other agreements. Pharmaceutical-grade drug substance for Dojolvi is manufactured by IOI Oleo pursuant to a supply agreement, and the drug product for Dojolvi is prepared by Haupt Pharma AG, pursuant to a master services agreement. Single source suppliers are also used for our gene therapy programs. We cannot provide assurances that identifying alternate sources, if available at all, 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. Additionally, we may not be able to enter into supply arrangements with an alternative supplier on commercially reasonable terms or at all. The terms of any new agreement 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.

***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.

**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. The COVID-19 pandemic has impacted and may continue to impact our ability to identify new patients and to maintain consistent contact with our current patients. For instance, illness from the more contagious variants impacted the availability of certain of our field and sales medical teams and resulted in staffing shortages at offices, clinics, and hospitals. Some of our current products or clinical programs may also be most appropriate for patients with more severe forms of their disease. For instance, 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. 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.

***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. See “Item 1. Business – Competition” above.

We have competitors both in the U.S. 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 may not be able to effectively manage the expansion of our organization, including building 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 increase our revenue.***

We expect to need additional managerial, operational, marketing, financial, legal, and other resources to support our development and commercialization plans and strategies. In order to successfully commercialize our products as well as any additional products that may result from our development programs or that we acquire or license from third parties, we are building

and expanding our commercial infrastructure in North America, Europe, Latin America and the Asia-Pacific region. 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. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We, as a company, have limited, recent experience selling and marketing our product and only some of our employees have prior experience promoting other similar products while employed at other companies. As we increase the number and range of our commercialized products, we may experience additional complexities in our sales process and strategy and may encounter difficulties in allocating sufficient resources to sales and marketing of certain products. Further, as we launch additional products or as demand for our products change, 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 larger 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 rights to promote Crysvita in the U.S. and Canada will transition back to KKC.***

Pursuant to the terms of our collaboration and license agreement with KKC, or the collaboration agreement, we have the sole right to promote Crysvita in the U.S. and Canada, or the profit-share territory, for a specified period of time, with KKC increasingly participating in the promotion of the product until the transition date of April 2023. At the transition date, commercialization responsibilities for Crysvita in the profit-share territory will transition to KKC, and KKC will be responsible for the commercialization of the product in the territory. In September 2022, we entered into an amendment to the collaboration agreement which clarified the scope of increased participation by KKC in support of our commercial activities prior to April 2023 and granted us the right to continue to support KKC in commercial field activities in the U.S. through April 2024, subject to the limitations and conditions set forth in the amendment. As a result, KKC will continue to support our commercial field and marketing efforts through a cost share arrangement through April 2024, subject to the limits and conditions set forth in the amendment. After April 2024, our rights to promote Crysvita in the U.S. will be limited to medical geneticists and we will be solely responsible for our costs related to the promotion of Crysvita in the profit-share territory. The transition of responsibilities to KKC requires significant effort and may result in the diversion of management’s attention to transition activities. We may also encounter unexpected difficulties or incur unexpected costs in connection with such transition activities. Further, we cannot assure that we will have adequate commercial activity to support our North America field force and other aspects of our commercial infrastructure in the territory after April 2024 and we may fail to retain members of our field teams due to such uncertainties. Collaboration with KKC may not result in a seamless

transition of responsibilities, and 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 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 continue to 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. In addition, we do not know the reimbursement rates until we are ready to market the product and we actually negotiate the rates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U.S., 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 U.S., 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 U.S., the reimbursement for our products may be reduced compared with the U.S. and may be insufficient to generate commercially reasonable revenue and profits. The timing to complete the negotiation process in each country is highly uncertain, and in some countries outside of the United States, we expect the process to exceed several months. Even if a price can be negotiated, countries frequently request or require reductions to the price and other concessions over time, including retrospective “clawback” price reductions. Additionally, member states of the EU have regularly imposed new or additional cost containment measures for pharmaceuticals such as volume discounts, cost caps, clawbacks and free products for a portion of the expected therapy period. For example, in France, we estimate clawback reserves on Dojolvi based on current regulations, our estimate of pricing on approval of Dojolvi and other factors. However, if pricing is approved at levels lower than estimated, if at all, or if there are further changes in the regulatory framework, we may be required to pay back amounts higher than clawback reserves and reverse revenue that has been previously recorded.

Moreover, increasing efforts by governmental and third-party payors in the U.S. 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, including the impact from the Inflation Reduction Act of 2022, and statements by elected officials. For example, proposals have been 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. Drug pricing is also expected to remain a focus for the current Presidential Administration and Congress. 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.

**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 U.S. and in other countries with respect to our proprietary technologies, our products, and our product candidates.

We have sought to protect our proprietary position by filing patent applications in the U.S. and abroad related to our novel technologies, products and product candidates 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 U.S. 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. Third parties may challenge the validity, enforceability, or scope of any issued patents 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.

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 could impair the exclusivity position of our products or deprive us of rights necessary for the successful commercialization of any product candidates that are approved. 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.

Our current patents or applications covering methods of use and certain compositions of matter do not provide 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 this product. 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 U.S., 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 or biosimilar medications.

Patent term extensions under the Hatch-Waxman Act in the U.S. and under supplementary protection certificates in Europe may not be available to extend the patent exclusivity term for our products and product candidates, and 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 U.S. 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 U.S. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. 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 in-licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions.

In 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law and introduced significant changes to the prosecution of U.S. patent applications and to the procedures for challenging U.S. patents. The effects of these changes still remain unclear owing to the evolving nature of the law and the lengthy timelines associated with court system review and interpretation. However, 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. The confidentiality agreements entered into with our employees, consultants, scientific advisors, contractors and other third parties that we rely on in connection with the development, manufacture and commercialization of our products may not be sufficient to protect our proprietary technology and processes, which increase the risk that such trade secrets may become known by our competitors or may be inadvertently incorporated into the technology of others.

The physical security of our premises and physical and electronic security of our information technology systems may not preserve the integrity and confidentiality of our data and trade secrets. 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.

The assignment agreements we enter into with our employees and consultants to assign their inventions to us, and the confidentiality agreements we enter into with our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information, or technology may not have been duly executed and we cannot assure 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 relevant 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 U.S. 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 are relevant to our products or product candidates.

We are aware of certain U.S. and foreign patents owned by third parties that a court might construe to be valid and relevant to one or more of our gene therapy product candidates, certain methods that may be used in their manufacture or delivery, or certain formulations comprising one or more of our gene therapy candidates. We are also aware of certain U.S. and foreign patents owned by third parties that relate to nucleic acid-containing lipid particles or to certain mRNA modifications, and which a court might construe to be valid and relevant to UX053. There is a risk that one or more of these third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that one or more of these patents is valid, enforceable, and infringed, in which case the owners of any such patents may be able to block our ability to commercialize a product candidate unless we obtained a license under the applicable patents, or until such patents expire. However, 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.***

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 the corresponding program.

***We may face competition from biosimilars, which may have a material adverse impact on the future commercial prospects of our biological products and product candidates.***

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 our biological products (Crysvita, Mepsevii and Evkeeza) and our biological product candidates. In the U.S., 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. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning are subject to uncertainty. 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 our biological products and product candidates.

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.

***Competitors could enter the market with generic versions of Dojolvi or our small-molecule product candidates, which may result in a material decline in sales of affected products.***

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, competitors could file ANDAs for generic versions of our small-molecule product, Dojolvi, or 505(b)(2) NDAs that reference Dojolvi. For the patents listed for Dojolvi 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 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 products and product candidates is dependent on third parties.***

While we normally seek and gain the right to fully prosecute the patents relating to our products or product candidates, there may be times when patents relating to our products or product candidates are controlled by our licensors. This is the case with our license agreements with KKC and Regeneron, who are primarily responsible for the prosecution of certain patents and patent applications covering Crysvita and Evkeeza, respectively.

In addition, we have in-licensed various patents and patent applications owned by the University of Pennsylvania relating to our DTX301,DTX401 and/or UX701 product candidates. Some of these patents and patent applications are licensed or sublicensed by REGENX 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 REGENX, 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, REGENX and the University of Pennsylvania may have interests which differ from ours in determining whether to enforce and the manner in which to enforce such patents.

We also have in-licensed patents and patent applications owned by Arcturus relating to the cationic lipid used in UX053. 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 Arcturus, we do not have the first right to enforce these patents, and our enforcement rights are subject to certain limitations that may adversely impact our ability to use these licensed patents to exclude others from commercializing competitive products. Moreover, Arcturus may have interests which differ from ours in determining whether to enforce and the manner in which to enforce such patents.

If KKC, Regeneron, the University of Pennsylvania, REGENX, Arcturus or any of our future licensing partners fail to appropriately prosecute, maintain, and enforce patent protection for the patents covering any of our products or product candidates, our ability to develop and commercialize those products or 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 product candidates.

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.

***We may become involved in lawsuits to protect or enforce our patents or the patents of our licensors, or be subject to claims that challenge the inventorship or ownership of our patents or other intellectual property, which could be expensive, time consuming, and result in unfavorable outcomes.***

Competitors may infringe our patents or the patents of our licensors. 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 U.S., 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.

We may in the future also be subject to claims that former employees, collaborators, or other third parties have an interest in our patents as an inventor or co-inventor. In addition, we may have ownership 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 or ownership. If we fail to successfully defend against such litigation or 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.

Even if we are successful in defending against such litigation and claims, such proceedings could result in substantial costs and distract our management and other employees. 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 litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments related to such litigation or claims. 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. Our efforts to vet our employees, consultants, and independent contractors and prevent their use of the proprietary information or know-how of others in their work for us may not be successful, and we may in the future be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties. 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.

***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 U.S. 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. Additionally, there have been recent proposals for additional changes to the patent laws of the U.S. 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 U.S. can be less extensive than those in the U.S. 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 U.S. Further, licensing partners such as KKC and Regeneron 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 U.S., or from selling or importing products made using our inventions in and into the U.S. 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 U.S. 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**

***We have no experience as a company developing or operating a manufacturing facility and may experience unexpected costs or delays or ultimately be unsuccessful in developing a facility.***

We are currently constructing our gene therapy manufacturing facility in Bedford, Massachusetts, which we currently expect to complete in 2023. We do not have experience as a company, however, in developing a manufacturing facility and we may experience unexpected costs or delays or ultimately be unsuccessful in developing the facility or manufacturing capability. Even if we successfully complete construction of the facility and the facility is operational, we cannot assure that the plant will be fully utilized at all times, particularly as we begin manufacturing operations. We will also incur significant expenses and costs to operate the facility. As we expand our commercial footprint to multiple geographies, we may establish multiple manufacturing facilities, which may lead to regulatory delays or prove costly. Even if we are successful, we cannot assure that such additional capacity will be required or that our investment will be recouped. Further, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, lack of capacity, labor shortages, natural disasters, power failures, program failures, actual or threatened public health emergencies, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy.

***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. Our new office work model (including the requirement at certain locations that employees work from our office on specified days), vaccination policy and other workforce actions taken in response to the COVID-19 pandemic has adversely impacted our ability to attract and retain certain employees or to recruit new qualified personnel. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. Over the last several years, we have also experienced certain executive leadership changes. Leadership transitions are inherently difficult to manage, cause uncertainty and disruption and could increase the likelihood of turnover of other key officers and employees. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis or any of other member of our executive leadership team or other key employee, 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 U.S., 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 Dojolvi for the treatment of fatty acid oxidation disorders in the U.S. and for various subtypes of LC-FAOD in Europe, as well as for Crysvita, Mepsevii, DTX301, DTX401 and UX701 in the U.S. 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.

***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., or Dimension, in November 2017, we have recorded on our Consolidated Balance Sheet intangible assets for in-process research and development, or IPR&D, related to DTX301 and DTX401. We also recorded an intangible asset related to our license from Regeneron for Evkeeza. 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 Consolidated Statement of Operations. We have not recorded any impairments related to our intangible assets through the end of December 31, 2022.

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

The success of our business depends upon our ability to identify, license, discover, develop, or commercialize additional product candidates in addition to the continued clinical testing, potential approval, and commercialization of our existing 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.

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

As described above in "Item 1. Business - Government Regulation" and in the Risk Factor above entitled " – *The insurance coverage and reimbursement status of newly approved products is uncertain*" 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. 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.

***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, privacy and security laws and regulations, and tax laws and regulations. In certain jurisdictions, these regulatory requirements may be more stringent than those in the U.S., and in other circumstances these requirements may be more stringent in the U.S.

In particular, 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; and patient and non-patient privacy regulations, including the GDPR and the California Consumer Privacy Act, or CCPA, including amendments from the California Privacy Rights Act, or CPRA, as described above in "Item 1. Business – Government Regulation". 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. For instance, one of our programs for sponsored genetic testing to help patients receive an accurate diagnosis is the subject of an ongoing review by applicable governmental authorities of compliance with various fraud and abuse laws; we cannot assure that such program, or our other operations or programs, will not be found to violate such laws.

The GDPR imposes a number of strict obligations and restrictions on the ability to process personal data of individuals, in particular with respect to special categories of personal data like health data (e.g., reliance on a legal basis, information to individuals, notification to relevant national data protection authorities in case of personal data breach and implementation of appropriate security measures). EU member states may also impose additional requirements in relation to special categories of personal data through their national legislation. In addition, the GDPR imposes specific restrictions on the transfer of personal data to countries outside of the EEA that are not considered by the European Commission as providing an adequate level of protection (including the U.S.). Appropriate safeguards are required to enable such transfers (e.g., reliance on standard contractual clauses and transfer risk assessments). There are also several compliance requirements under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and implementing regulations that create requirements relating to the privacy and security of protected health information. Those requirements are also applicable, in many instances, to business associates of covered entities. In some cases, depending on our business operations and contractual agreements, including through the conduct of clinical trials, we are subject to HIPAA requirements. Also, we may be subject to additional federal, state and local privacy laws and regulations in the U.S., including new and recently enacted laws (such as CCPA and CPRA), that may apply to us and/or our service providers now or in the future and that require that we take measures to be transparent regarding, honor rights with respect to, and protect the privacy and security of certain information we gather and use in our business, including personal information, particularly personal information that is not otherwise subject to HIPAA.

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, disgorgement of profits, and the curtailment or restructuring of our operations. 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.

Our research and development activities, including our process and analytical development activities in our quality control laboratory, 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.

Additionally, as we and our employees increasingly use social media tools as a means of communication with the public, there is a risk that the use of social media by us or our employees to communicate about our products or business may cause to be found in violation of applicable laws, despite our attempts to monitor such social media communications through company policies and guidelines. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our company policies or other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property, cause reputational harm or result in public exposure of personal information of our employees, clinical trial patients, customers, and others.

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

Our business strategy includes international expansion. We currently conduct clinical studies and regulatory activities and we also commercialize products outside of the U.S. 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, additional or more burdensome regulatory requirements of financial institutions outside of the U.S., 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 geopolitical and economic instability, including wars, terrorism, political unrest (including, for example the conflict between Russia and Ukraine and the rising tensions between China and Taiwan), results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease (including for example, the COVID-19 pandemic), rising inflation, the potential recessionary environment, boycotts and resulting staffing shortages, 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.

***Risks generally associated with the expansion of our enterprise resource planning. or 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 expanding our company-wide ERP system to upgrade certain existing business, operational, and financial processes related to our gene therapy manufacturing facility, which we currently expect to be completed in 2023. The ERP expansion is a complex and time-consuming project. Our results of operations could be adversely affected if we experience time delays or cost overruns during the ERP expansion 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 expanded 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.***

Cybersecurity incidents, including phishing attacks and attempts to misappropriate or compromise confidential or proprietary information or sabotage enterprise IT systems are becoming increasingly frequent and more sophisticated. The information and data processed and stored in our technology systems, and those of our strategic partners, CROs, contract manufacturers, suppliers, distributors or other third parties for which we depend to operate our business, may be vulnerable to loss, damage, denial-of-service, unauthorized access or misappropriation. Data security breaches can occur as a result of malware, hacking, business email compromise, ransomware attacks, phishing or other cyberattacks directed by third parties. We, and certain of the third parties for which we depend on to operate our business, have experienced cybersecurity incidents, including third party unauthorized access to and misappropriation of financial information. Further, risks of unauthorized access and cyber-attacks have increased as most of our personnel, and the personnel of many third-parties with which we do business, have adopted flexible working arrangements as a result of the COVID-19 pandemic. Improper or inadvertent behavior by employees, contractors and others with permitted access to our systems, pose a risk that sensitive data may be exposed to unauthorized persons or to the public. A system failure or security breach that interrupts our operations or the operations at one of our third-party vendors or partners could result in intellectual property and other proprietary or confidential information being lost or stolen or a material disruption of our drug development programs and commercial operations. 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 information 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. Further, we could incur significant costs to investigate and mitigate such cybersecurity incidents. A security breach that results in the unauthorized access, use or disclosure of personal information also requires us to notify individuals, governmental authorities, credit reporting agencies, or other parties, as applicable, pursuant to privacy and security laws and regulations or other obligations. Such a security breach could harm our reputation, erode confidence in our information security measures, and lead to regulatory scrutiny and result in penalties, fines, indemnification claims, litigation and potential civil or criminal liability.

***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. We have also experienced power outages as a result of wildfires in the San Francisco Bay Area which are likely to continue to occur in the future. 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, or result in fluctuations with respect to the value of such investment, which could impact our operating results.***

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 GeneTx in July 2022. 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. We may experience difficulties in assimilating the personnel, operations and products of the acquired companies, management's attention may be diverted from other business concerns and we may potentially lose key employees of the acquired company. If we are unable to successfully or timely integrate the operations of acquired companies with our business, we may incur unanticipated liabilities and be unable to realize the revenue growth, synergies and other anticipated benefits resulting from the acquisition, and our business, results of operations and financial condition could be materially and adversely affected.

The value of our investments in other companies or businesses may also fluctuate significantly and impact our operating results quarter to quarter or year to year. For instance, in June 2019, we purchased 2,400,000 shares of common stock of Arcturus and in May 2020, we exercised our option to purchase an additional 600,000 shares of Arcturus' common stock pursuant to the terms of our equity purchase agreement with Arcturus; we have sold all our shares as of December 31, 2022. We also purchased 7,825,797 shares of common stock of Solid in October 2020. We have elected to apply the fair value option to account for our equity investments in Arcturus and Solid. As a result, increases or decreases in the stock price of equity investments have resulted in and will result in accompanying changes in the fair value of our investments, and cause substantial volatility in, our operating results for the reporting period. As the fair value of our investment in Solid is dependent on the stock price of Solid, which has recently seen wide fluctuations, the value of our investments and the impact on our operating results may similarly fluctuate significantly from quarter to quarter and year to year such that period-to-period comparisons may not be a good indication of the future value of the investments and our future operating results.

**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 investigations, regulatory proceedings or 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, macroeconomic conditions or geopolitical developments, including the impact from the COVID-19 pandemic, rising inflation and the potential recessionary environment;
- 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, 2022, there were 2,227,385 shares 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 the 2014 ESPP, eligible employees can acquire shares of our common stock at a discount to the prevailing market price. At December 31, 2022, there were 4,585,921 shares 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.

In February 2021, our board of directors adopted the Employment Inducement Plan, or the Inducement Plan, with a maximum of 500,000 shares available for grant under the plan. At December 31, 2022, there were 247,369 shares available for issuance under the Inducement Plan. If our board of directors elects to increase the number of shares available for future grant under the 2014 Plan, the 2014 ESPP, or the Inducement Plan, our stockholders may experience additional dilution, which could cause our stock price to fall.

***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.

**General Risk Factors**

***If we are unable to maintain 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. Section 404(b) of the Sarbanes-Oxley Act also requires our independent auditors to attest to, and report on, this management assessment. Ensuring that we have adequate internal controls in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to attest to the effectiveness of our internal control over financial reporting, 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.

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

We have a multinational tax structure and are subject to income tax in the U.S. 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.

***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.

***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, claims and proceedings in the ordinary course of business relating to our directors, officers, stockholders, intellectual property, and employment matters and policies, 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 claims or 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 claims or 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.

***Our business and operations could be negatively affected if we become subject to stockholder activism or hostile bids, which could cause us to incur significant expense, hinder execution of our business strategy and impact our stock price.***

Stockholder activism, which takes many forms and arises in a variety of situations, has been increasingly prevalent. Stock price declines may also increase our vulnerability to unsolicited approaches. If we become the subject of certain forms of stockholder activism, such as proxy contests or hostile bids, the attention of our management and our board of directors may be diverted from execution of our strategy. Such stockholder activism could give rise to perceived uncertainties as to our future strategy, adversely affect our relationships with business partners and make it more difficult to attract and retain qualified personnel. Also, we may incur substantial costs, including significant legal fees and other expenses, related to activist stockholder matters. Our stock price could be subject to significant fluctuation or otherwise be adversely affected by the events, risks and uncertainties of any stockholder activism.

***Increased scrutiny regarding ESG practices and disclosures could result in additional costs and adversely impact our business and reputation.***

Companies across all industries are facing increasing scrutiny relating to their Environmental, Social and Governance, or "ESG," practices and disclosures and institutional and individual investors are increasingly using ESG screening criteria in making investment decisions. Our disclosures on these matters or a failure to satisfy evolving stakeholder expectations for ESG practices and reporting may potentially harm our reputation and impact employee retention and access to capital. In addition, our failure, or perceived failure, to pursue or fulfill our goals, targets, and objectives or to satisfy various reporting standards within the timelines we announce, or at all, could expose us to government enforcement actions and private litigation.

Our ability to achieve any goal or objective, including with respect to environmental and diversity initiatives and compliance with ESG reporting standards, is subject to numerous risks, many of which are outside of our control. Examples of such risks include the availability and cost of technologies and products that meet sustainability and ethical supply chain standards, evolving regulatory requirements affecting ESG standards or disclosures, our ability to recruit, develop, and retain diverse talent in our labor markets, and our ability to develop reporting processes and controls that comply with evolving standards for identifying, measuring and reporting ESG metrics. As ESG best-practices, reporting standards, and disclosure requirements continue to develop, we may incur increasing costs related to maintaining or achieving our ESG goals in addition to ESG monitoring and reporting.

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

None.

**Item 2.** ***Properties***

Our primary operations are conducted at the leased facilities summarized in the below table. In 2020, we completed our purchase of land located in Bedford, Massachusetts and we are currently in the process of completing construction of our gene therapy manufacturing facility. 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.

| Property Location | Use | Lease Expiration Date |
|---|---|---|
| Novato, California | Headquarters and office | December 2024 |
| Novato, California | Laboratory and office | October 2028 |
| Brisbane, California | Office | June 2026 |
| South San Francisco, California | Laboratory and office | March 2025 |
| Cambridge, Massachusetts | Laboratory and office | December 2023 |
| Woburn, Massachusetts | Laboratory and office | April 2025 |
| Woburn, Massachusetts | Laboratory and office | October 2026 |
| Bedford, Massachusetts | Manufacturing facility | Owned property |

**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.

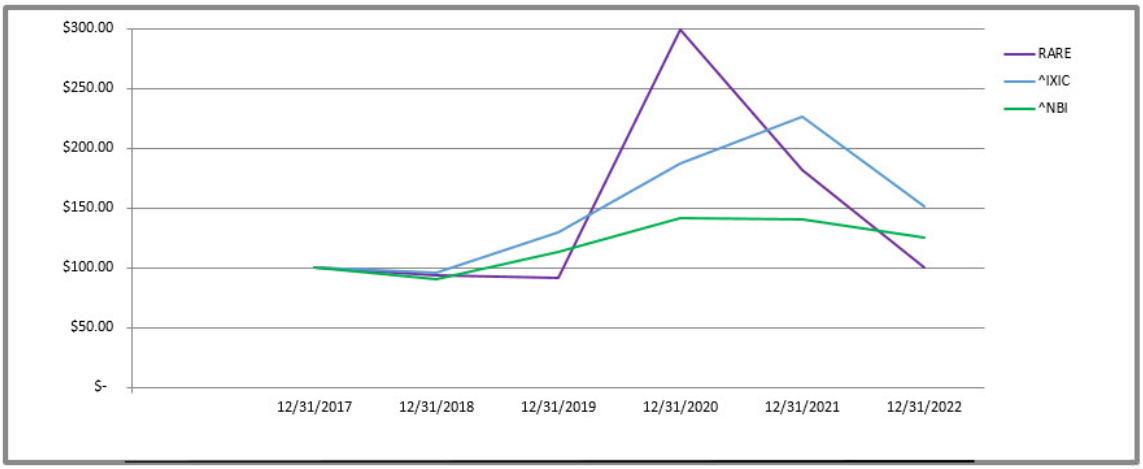
## PART II

**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 13, 2023, we had 7 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 (ii) the Nasdaq Biotechnology Index for the period from December 31, 2017 through December 31, 2022. The figures represented below assume an investment of $100 in our common stock at the closing price of $46.38 on December 31, 2017 and in the Nasdaq Composite Index, or IXIC, and the Nasdaq Biotechnology Index, or NBI, on December 31, 2017 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 the 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, 2017 | December 31, 2018 | December 31, 2019 | December 31, 2020 | December 31, 2021 | December 31, 2022 |
|---|---|---|---|---|---|---|---|
| Ultragenyx Pharmaceutical Inc. | RARE | $ 100.00 | $ 93.75 | $ 92.09 | $ 298.47 | $ 181.31 | $ 99.89 |
| NASDAQ Composite Index | ^IXIC | $ 100.00 | $ 96.12 | $ 129.97 | $ 186.69 | $ 226.63 | $ 151.61 |
| NASDAQ Biotechnology Index | ^NBI | $ 100.00 | $ 90.68 | $ 112.81 | $ 141.78 | $ 140.88 | $ 125.52 |

### 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.** ***Reserved***

**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 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, 2022, including year-over-year comparisons versus the year ended December 31, 2021. Our Annual Report on Form 10-K for the year ended December 31, 2021 includes a discussion and analysis of our financial condition and results of operations for the year ended December 31, 2020 in "Part II, Item 7. 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 four product categories: biologics, small molecules, gene therapy, and nucleic acid product candidates. We have four commercially approved products, consisting of Crysvita® (burosumab) for the treatment of X-linked hypophosphatemia, or XLH, and tumor-induced osteomalacia, or TIO, Mepsevii® (vestronidase alfa) for the treatment of mucopolysaccharidosis VII, or MPSVII or Sly Syndrome, Dojolvi® (triheptanoin) for the treatment of long-chain fatty acid oxidation disorders, or LC-FAOD, and Evkeeza® (evinacumab) for the treatment of homozygous familial hypercholesterolemia, or HoFH. Please see "Item 1. Business" above for a description of our approved products and our clinical stage pipeline products.

### 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 our equity securities, revenues from our commercial products, the sale of certain future royalties, and strategic collaboration arrangements.

We have incurred net losses in each year since inception. Our net losses were $707.4 million and $454.0 million for the years ended December 31, 2022 and 2021, respectively. Net loss for the years ended December 31, 2022 and 2021 included losses of $19.3 million and $42.1 million, respectively, resulting from changes in fair value of our investments in Arcturus Therapeutics Holdings Inc., or Arcturus, and Solid Biosciences Inc., or Solid, equity securities. 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.

For the year ended December 31, 2022, our total revenues increased to $363.3 million, compared to $351.4 million for the same period in 2021. The increase was driven by higher Crysvita collaboration revenue in the profit-share territory, increase in revenue for our approved products, and an increase in collaboration royalty revenue, partially offset by a decrease in collaboration and license revenue from the Daiichi Sankyo arrangement.

As of December 31, 2022, we had $896.7 million in available cash, cash equivalents and marketable debt securities.

**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 GAAP accounting principles 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:

***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, or 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. We record our share of collaboration revenue, net of transfer pricing related to net sales in the period in which such sales occur, if we are considered as an agent in the arrangement. We are considered an agent when the collaboration partner controls the product before transfer to the customers and has the ability to direct the use of and obtain substantially all of the remaining benefits from the product. 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 our ongoing major or central operations.

We also record 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 material changes to prior period estimates of revenues and expenses.

We sold the right to receive certain royalty payments from net sales of Crysvita in certain territories to RPI Finance Trust, or RPI, an affiliate of Royalty Pharma, and to OCM LS23 Holdings LP, an investment vehicle for Ontario Municipal Employees Retirement System, or OMERS, as further described in “Liabilities for Sales of Future Royalties” below. We record the royalty revenue from the net sales of Crysvita in the applicable territories on a prospective basis as non-cash royalty revenue in the Consolidated Statements of Operations over the term of the applicable arrangement.

The terms of our collaboration and license 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, or* ASC 606, 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 our relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. We estimate the efforts needed to complete the performance obligations and recognizes revenue by measuring the progress towards complete satisfaction of the performance obligations using input measures.

*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. Our estimates of government mandated rebates, chargebacks, estimated product returns, and other deductions depends on the identification of key customer contract terms and conditions, as well as estimates of sales volumes to different classes of payors. If actual results vary, we may need to adjust these estimates, which could have a material 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 costs begins when we have received the regulatory approval of the product. Prior to the FDA approval of our products, manufacturing and related costs were expensed; accordingly, these costs were not capitalized and as a result are not reflected in the costs of sales after the regulatory approval date. As of December 31, 2022, we do not hold a material amount of previously expensed inventory for our approved products.

Inventory that is manufactured after regulatory approval is valued at the lower of cost and net realizable value and cost is determined using the average-cost method.

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

***Liabilities for Sales of Future Royalties***

In December 2019, we entered into a Royalty Purchase Agreement with RPI. Pursuant to the agreement, RPI paid us $320.0 million in consideration for our right to receive royalty payments on the net sales of Crysvita in the EU, 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.

In July 2022, we entered into a Royalty Purchase Agreement with OMERS. Pursuant to the agreement, OMERS paid $500.0 million to us in consideration for the right to receive 30% of the future royalty payments due to us from KKC based on net sales of Crysvita in the U.S. and Canada under the terms of the KKC Collaboration Agreement. The calculation of royalty payments to OMERS will be based on net sales of Crysvita beginning in April 2023 and will expire upon the earlier of the date on which aggregate payments received by OMERS equals $725.0 million or the date the final royalty payment is made to us under the KKC Collaboration Agreement.

Proceeds from these transactions were recorded as liabilities (specifically, liabilities for sales of future royalties on the Consolidated Balance Sheets). We are amortizing $320.0 million and $500.0 million, net of transaction costs of $5.8 million and $9.1 million for RPI and OMERS, respectively, using the effective interest method over the estimated life of the applicable arrangement. In order to determine the amortization of the liabilities, we are required to estimate the total amount of future royalty payments to be received by us and paid to RPI and OMERS, subject to the capped amount, over the life of the arrangements. The excess of future estimated royalty payments (subject to the capped amount), in excess of the net proceeds received of $314.2 million and $491.0 million, respectively, is recorded as non-cash interest expense over the life of the arrangements. Consequently, we estimate an imputed interest on the unamortized portion of the liabilities and record interest expense relating to the transactions. We record the royalty revenue arising from the net sales of Crysvita in the applicable territories as non-cash royalty revenue in the Consolidated Statements of Operations over the term of the arrangements.

We periodically assess 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 our initial estimates or the timing of such payments is materially different than its original estimates, we will prospectively adjust the amortization of the liabilities and the effective interest rate. Our effective annual interest rate was approximately 9.3% and 8.4%, for RPI and OMERS, respectively, as of December 31, 2022.

There are a number of factors that could materially affect the amount and timing of royalty payments from KKC in the applicable 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, delays or disruptions related to the COVID-19 pandemic, macroeconomic and inflationary pressures, the introduction of competing products, pricing for reimbursement in various 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, or USD, while significant portions of the underlying sales of Crysvita are made in currencies other than USD, and other events or circumstances that could result in reduced royalty payments from 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 the relevant territories are more than expected, the non-cash royalty revenue and the non-cash interest expense recorded by us would be greater over the term of the arrangements.

***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 equity awards 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.

Strike price for options, including performance stock options, or PSOs, is equal to the closing market value of our common stock on the date of grant.

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, or RSUs, and performance stock units, or PSUs, the fair value is based on the market value of our common stock on the date of grant, except for certain PSUs with a market vesting condition, for which fair value is estimated using a Monte Carlo simulation model. 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, including both performance conditions and market conditions. 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, 2022, 2021, and 2020 stock-based compensation expense was $130.4 million, $105.0 million, and $85.7 million, respectively. As of December 31, 2022, we had $229.4 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 2.28 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 in 2017, 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, 2022, our total gross deferred tax assets were $900.7 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating losses and tax credit carryforwards. Utilization of the net operating loss and tax credit carryforwards may be subject to an annual limitation due to

historical or future ownership percentage change rules provided by the Internal Revenue Code of 1986, and similar state provisions. The annual limitation may result in the expiration of certain net operating loss and tax credit carryforwards before their utilization.

**Results of Operations**

***Comparison of Years Ended December 31, 2022 and 2021***

*Revenues (dollars in thousands)*

| | Year Ended December 31, | | Dollar | Percent |
|---|---|---|---|---|
| | 2022 | 2021 | Change | Change |
| Collaboration and license revenue: | | | | |
| Crysvita collaboration revenue in profit-share territory | $ 215,024 | $ 171,198 | $ 43,826 | 26% |
| Crysvita royalty revenue in European territory | — | 244 | (244) | (100%) |
| Daiichi Sankyo | 7,686 | 84,996 | (77,310) | (91%) |
| Total collaboration and license revenue | 222,710 | 256,438 | (33,728) | (13%) |
| Product sales: | | | | |
| Crysvita | 42,678 | 21,422 | 21,256 | 99% |
| Mepsevii | 20,637 | 16,035 | 4,602 | 29% |
| Dojolvi | 55,612 | 39,560 | 16,052 | 41% |
| Total product sales | 118,927 | 77,017 | 41,910 | 54% |
| Crysvita non-cash collaboration royalty revenue | 21,692 | 17,951 | 3,741 | 21% |
| Total revenues | $ 363,329 | $ 351,406 | $ 11,923 | 3% |

For the year ended December 31, 2022, our share of Crysvita collaboration revenue in the profit-share territory increased by $43.8 million, as compared to the same period in 2021. The increase was primarily due to continued increase in demand for Crysvita due to an increase in the number of patients on therapy.

For the year ended December 31, 2022, the collaboration and license revenue from our license agreement with Daiichi Sankyo decreased by $77.3 million, as compared to the same period in 2021. The decrease was due to the completion of the technology transfer as of March 31, 2022.

The increase in product sales of $41.9 million for the year ended December 31, 2022, compared to the same period in 2021 was primarily due to an increase in demand for Crysvita in Latin America due to an increase in the number of patients on therapy, continued momentum from the commercial launch of Dojolvi in the U.S., continued increase in demand for our other approved products, and an increase in sales of our products under our named patient program in certain countries.

The increase in Crysvita non-cash collaboration royalty revenue of $3.7 million for the year ended December 31, 2022, compared to the same period in 2021, was primarily due to the launch progress by our collaboration partner in European countries and an increase in the number of patients on therapy.

*Cost of Sales (dollars in thousands)*

| | Year Ended December 31, | | Dollar | Percent |
|---|---|---|---|---|
| | 2022 | 2021 | Change | Change |
| Cost of sales | $ 28,320 | $ 16,008 | $ 12,312 | 77% |

Cost of sales related to our approved products increased by $12.3 million for the year ended December 31, 2022, compared to the same period in 2021. The increase was due to increased demand for our approved products and amortization of the intangible asset for Evkeeza from our license agreement with Regeneron, which began in January 2022.

*Research and Development Expenses (dollars in thousands)*

Research and development expenses include internal and external costs incurred for research and development of our programs and program candidates and expenses related to certain technology that we acquire or license through business development transactions. These expenses consist primarily of clinical studies performed by contract research organizations, manufacturing of drug substance and drug product performed by contract manufacturing organizations, materials and supplies, fees from collaborative and other arrangements including milestones, licenses and other fees, personnel costs including salaries, benefits and stock-based compensation, and overhead allocations consisting of various support and infrastructure costs.

Commercial programs include costs for disease monitoring programs and certain regulatory and medical affairs support activities for programs after commercial approval. Clinical programs include study conduct and manufacturing costs related to clinical program candidates. Translational research includes costs for preclinical study work and costs related to preclinical programs prior to IND filing. Upfront license, acquisition, and milestone fees include any significant expenses related to strategic licensing agreements and acquisitions. Infrastructure costs include direct costs related to laboratory, IT, and equipment depreciation costs, and overhead allocations for human resources, IT, and other allocable costs.

The following table provides a breakout of our research and development expenses by major program type and business activities:

| | Year Ended December 31, | | Dollar Change | Percent Change |
|---|---|---|---|---|
| | 2022 | 2021 | | |
| Commercial programs | $ 75,683 | $ 52,015 | $ 23,668 | 46% |
| Clinical programs: | | | | |
| Gene therapy programs | 153,754 | 108,217 | 45,537 | 42% |
| Nucleic acid and other biologic programs | 97,268 | 50,681 | 46,587 | 92% |
| Translational research | 81,431 | 62,207 | 19,224 | 31% |
| Upfront license, acquisition, and milestone fees | 75,033 | 50,000 | 25,033 | 50% |
| Infrastructure | 71,657 | 59,294 | 12,363 | 21% |
| Stock-based compensation | 74,464 | 59,097 | 15,367 | 26% |
| Other research and development | 76,499 | 55,642 | 20,857 | 37% |
| Total research and development expenses | $ 705,789 | $ 497,153 | $ 208,636 | 42% |

Total research and development expenses increased $208.6 million for the year ended December 31, 2022 compared to the same period in 2021. The change in research and development expenses was due to:

- for commercial programs, an increase of $23.7 million, primarily related to the cost sharing for ongoing clinical trials with Regeneron for Evkeeza, new Evkeeza regulatory and medical affairs support activities, and increased R&D personnel allocations to commercial programs;
- for gene therapy programs, an increase of $45.5 million, primarily related to increases in clinical manufacturing and clinical trial expenses for our Phase 3 programs for DTX401 and DTX301 and development costs related to the UX111 program from Abeona Therapeutics;
- for nucleic acid and other biologic programs, an increase of $46.6 million, primarily related to the addition of clinical trial expenses related to UX053, following its IND approval in March 2021; increased clinical trial and manufacturing expenses related to the continued progress of the UX143 program in collaboration with Mereo; and clinical and other development expenses related to the continued progress of the GTX-102 program;
- for translational research, an increase of $19.2 million, primarily related to IND-enabling development costs for multiple research projects;
- for upfront license, acquisition, and milestone fees, an increase of $25.0 million, primarily due to $75.0 million recognized from the GeneTx acquisition for the year ended December 31, 2022, as compared $50.0 million recognized from the upfront fee for the Mereo license for the year ended December 31, 2021;
- for infrastructure, an increase of $12.4 million, primarily related to increased expenses for support of our clinical and research program pipeline, expansion of laboratory space, depreciation of laboratory-related leasehold improvements and equipment, and IT-related expenses;
- for stock-based compensation, an increase of $15.4 million, primarily related to the increased employee headcount; and
- for other research and development expenses, an increase of $20.9 million, primarily related to increased staffing to support internal manufacturing, increased travel, and increased administrative and general support.

We expect our annual research and development expenses to moderate 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 | Percent |
|---|---|---|---|---|
| | 2022 | 2021 | Change | Change |
| Selling, general and administrative | $ 278,139 | $ 219,982 | $ 58,157 | 26% |

Selling, general and administrative expenses increased $58.2 million for the year ended December 31, 2022, compared to the same period in 2021. The increases in selling, general and administrative expenses were primarily due to increases in personnel costs resulting from an increase in the number of employees to support our commercial activities, commercialization costs, and professional services costs.

We expect selling, general and administrative expenses to moderate in the future as we continue to support our approved products and multiple clinical-stage product candidates, with expected decreases in commercial activities due to transition of Crysvita to our partner in the profit-share territory.

*Interest Income (dollars in thousands)*

| | Year Ended December 31, | | Dollar | Percent |
|---|---|---|---|---|
| | 2022 | 2021 | Change | Change |
| Interest income | $ 11,074 | $ 1,928 | $ 9,146 | 474% |

Interest income increased $9.1 million for the year ended December 31, 2022 compared to the same period in 2021, primarily due to increases in interest rates and higher average marketable debt securities balances.

*Change in Fair Value of Equity Investments (dollars in thousands)*

| | Year Ended December 31, | | Dollar | Percent |
|---|---|---|---|---|
| | 2022 | 2021 | Change | Change |
| Change in fair value of equity investments | $ (19,299) | $ (42,063) | $ 22,764 | (54%) |

For the year ended December 31, 2022, we recorded a net decrease in the fair value of our equity investments of $19.3 million. The fair value of our investments in Arcturus and Solid common stock decreased by $8.4 million and $10.9 million, respectively, for the period. The change in fair value of Arcturus included a realized gain on the sale of all our remaining shares of common stock for net proceeds of $10.1 million.

For the year ended December 31, 2021, we recorded a net decrease in the fair value of our equity investments of $42.1 million. The fair value of our investment in Solid common stock decreased by $45.6 million for the period. This was offset by an increase in the fair value of our investment in Arcturus common stock of $2.9 million for the period, which included a realized gain on the sale of a portion of Arcturus common stock for net proceeds of $79.8 million, as well as an increase of $0.6 million related to the conversion of the convertible note in a private pharmaceutical company to its preferred shares, resulting in a net decrease in the fair value of equity investments of $42.1 million.

Given the historic volatility of the publicly traded stock price of Solid, the fair value adjustments of our equity investments may be subject to wide fluctuations which may have a significant impact on our earnings in future periods.

*Non-cash Interest Expense on Liabilities for Sales of Future Royalties (dollars in thousands)*

| | Year Ended December 31, | | Dollar | Percent |
|---|---|---|---|---|
| | 2022 | 2021 | Change | Change |
| Non-cash interest expense on liabilities for sales of future royalties | $ 43,015 | $ 29,422 | $ 13,593 | 46% |

Our non-cash interest expense on liabilities for sales of future royalties increased by $13.6 million for the year ended December 31, 2022, compared to the same period in 2021. This was primarily due to the partial sale of North American Crysvita royalties to OMERS in July 2022, which resulted in an increase in liabilities for sales of future royalties by $491.0 million and higher interest expense, partially offset by an increase of $6.7 million in the capitalization of interest related to the construction-in-progress for the gene therapy manufacturing plant, compared to the same period in 2021. To the extent royalty payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, we will prospectively adjust the effective interest rate.

*Other Expense (dollars in thousands)*

| | Year Ended December 31, | | Dollar | Percent |
|---|---|---|---|---|
| | 2022 | 2021 | Change | Change |
| Other expense | $ (1,566) | $ (1,687) | $ 121 | (7%) |

Other expense decreased $0.1 million for the year ended December 31, 2022, compared to the same period in 2021. These changes were primarily due to fluctuations in foreign exchange rates.

*Provision for income taxes*

| | Year Ended December 31, | | Dollar | Percent |
|---|---|---|---|---|
| | 2022 | 2021 | Change | Change |
| Provision for income taxes | $ (5,696) | $ (1,044) | $ (4,652) | 446% |

The provision for incomes taxes increased by $4.7 million for the year ended December 31, 2022, compared to the same period in 2021. Beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminated the ability to deduct research and development expenditures for tax purposes in the period the expenses were incurred and instead requires all U.S. and foreign research and development expenditures to be amortized over five and fifteen tax years, respectively. Due to this required capitalization of research and development expenditures and the significant taxable income generated as a result of our sale of royalties in July 2022, we have recorded a one-time discrete state tax expense of $6.1 million for the year ended December 31, 2022. The discrete tax expense is for state taxes we anticipate paying as a result of statutory limitations on our ability to offset expected taxable income with net operating loss carry forwards in certain states. We realized no benefit for current year losses due to a full valuation allowance against the U.S. net deferred tax assets.

**Liquidity and Capital Resources**

To date, we have funded our operations primarily from the sale of our equity securities, revenue from our commercial products, the sale of certain future royalties, and strategic collaboration arrangements.

As of December 31, 2022, we had $896.7 million in available cash, cash equivalents, and marketable debt securities. 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 marketable debt securities are held in a variety of deposit accounts, interest-bearing accounts, corporate bond securities, commercial paper, U.S government securities, asset-backed securities, debt securities in government-sponsored entities, 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.

In May 2021, we entered into an Open Market Sale Agreement with Jefferies LLC, or Jefferies, pursuant to which we may offer and sell shares of our common stock having an aggregate offering proceeds up to $350.0 million, from time to time, in at-the-market, or ATM, offerings through Jefferies. As of December 31, 2022, net proceeds from shares sold under the arrangement were approximately $78.9 million. No shares were sold under this arrangement for the year ended December 31, 2022.

In July 2022, we received net proceeds of $491.0 million from the sale of certain future royalties to OMERS.

For the year ended December 31, 2022, we sold all of our remaining 500,000 shares of Arcturus common stock for net proceeds of $10.1 million.

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Cash used in operating activities | $ (380,465) | $ (338,695) | $ (132,220) |
| Cash used in investing activities | (291,652) | (195,372) | (179,121) |
| Cash provided by financing activities | 501,208 | 118,552 | 600,272 |
| Effect of exchange rate changes on cash | (1,075) | (1,194) | 1,119 |
| Net (decrease) increase in cash, cash equivalents, and restricted cash | $ (171,984) | $ (416,709) | $ 290,050 |

***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, 2022 was $380.5 million and primarily reflected a net loss of $707.4 million and $21.7 million for non-cash collaboration royalty revenues related to the sale of future royalties to RPI, offset by non-cash charges of $130.4 million for stock-based compensation, $75.0 million for acquired in-process research and development expense, $2.7 million for the amortization of the premium paid on marketable debt securities, $18.2 million for depreciation and amortization, $19.3 million primarily for the net change in fair value of equity investments from Arcturus and Solid, and $43.0 million for non-cash interest expense incurred on the liabilities for sales of future royalties to RPI and OMERS, net of capitalized interest. Cash used in operating activities also reflected a $12.1 million decrease due to an increase in accounts receivable primarily related to an increase in sales of our approved products, a $9.7 million decrease due to an increase in inventory for Mepsevii and Dojolvi, a decrease of $7.6 million in contract liabilities, net, related to the revenue recognized from the license agreements with Daiichi Sankyo, and a decrease of $1.6 million due to a decrease in deferred tax liabilities, related to certain changes in tax law requiring capitalization of research and development expenses combined with taxable income generated by our sale of future royalties to OMERS. These decreases were offset by a $3.8 million increase in prepaid expenses and other assets primarily due to a decrease in prepaid fixed assets, and a $87.4 million increase in accounts payable, accrued liabilities, and other liabilities primarily due to timing of payments and receipt of invoices, as well as an increase in manufacturing accruals related to manufacturing and clinical expenses, an increase in accrued bonus due to an increase in headcount, and an increase in accrued development costs owed to a collaboration partner.

Cash used in operating activities for the year ended December 31, 2021 was $338.7 million and primarily reflected a net loss of $454.0 million and $18.0 million for non-cash collaboration royalty revenues related to the sale of future royalties to RPI, offset by non-cash charges of $105.0 million for stock-based compensation, $13.2 million for depreciation and amortization, $6.6 million for the amortization of the premium paid on marketable debt securities, $42.1 million primarily for the net change in fair value of equity investments from Arcturus and Solid, and $29.4 million for non-cash interest expense incurred on the liability for sales of future royalties to RPI, net of capitalized interest. Cash used in operating activities also reflected a $5.4 million decrease due to an increase in accounts receivable primarily related to higher revenues, a $3.1 million decrease due to an increase in inventory for Dojolvi, a $29.5 million decrease due to an increase in prepaid expenses and other assets primarily due to an increase in prepaid manufacturing expenses, prepaid clinical expenses, and prepaid fixed assets as well as an increase in receivables from our collaboration partner, and a decrease of $57.5 million in contract liabilities, net, related to the revenue recognized from the license agreements with Daiichi Sankyo. These decreases were offset by a $32.3 million increase in accounts payable, accrued liabilities, and other liabilities primarily due to an increase in accruals related to manufacturing expenses, compensation related expenses, collaboration expenses and income taxes payable.

***Cash Used in Investing Activities***

Cash used in investing activities for the year ended December 31, 2022 was $291.7 million and was primarily related to purchases of property, plant, and equipment of $116.1 million, primarily related to the construction of our gene therapy manufacturing facility, the acquisition of GeneTx for $75.0 million, net of cash acquired, purchases of marketable debt securities of $614.7 million, and the payment to Regeneron for intangible assets of $30.0 million offset by the sale of marketable debt securities of $84.3 million, proceeds from the sale of Arcturus common stock of $10.1 million, and proceeds from maturities of marketable debt securities of $450.7 million.

Cash used in investing activities for the year ended December 31, 2021 was $195.4 million and was primarily related to purchases of property, plant, and equipment of $73.1 million and purchases of marketable debt securities of $1,012.2 million, offset by the sale of marketable debt securities of $92.9 million, proceeds from the sale of Arcturus common stock of $79.8 million, and proceeds from maturities of marketable debt securities of $718.1 million.

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

Cash provided by financing activities for the year ended December 31, 2022 was $501.2 million and was comprised of $491.0 million in net proceeds from the partial sale of future North America Crysvita royalties to OMERS and $10.8 million in net proceeds from the issuance of common stock upon the exercise of stock options, net of taxes withheld from the vesting of restricted stock units.

Cash provided by financing activities for the year ended December 31, 2021 was $118.6 million and was comprised of $78.9 million in net proceeds from the issuance of common stock from our ATM offering and $40.1 million in net proceeds from the issuance of common stock upon the exercise of stock options, net of taxes withheld from the vesting of restricted stock units.

**Funding Requirements**

We anticipate that, excluding non-recurring items, 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 require additional capital to fund our operations, to complete our ongoing and planned clinical studies, to commercialize our products, to continue investing in early-stage research capabilities to promote our pipeline growth, to continue to acquire or invest in businesses or products that complement or expand our business, including future milestone payments thereunder, and to further develop our general infrastructure, including construction of our 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, products that we have begun to commercialize, and any products that we may develop in the future, including the construction 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;
- the magnitude and extent to which the COVID-19 pandemic impacts our business operations and operating results, as described in “Part I, Item IA. Risk Factors " and
- the terms and timing of any collaborative, licensing, marketing, distribution, acquisition 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, revenue from our commercial products, and a 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 and Commitments**

Material contractual obligations arising in the normal course of business primarily consist of operating and finance leases, and manufacturing and service contract obligations. See Note 9 to the Consolidated Financial Statements for amounts outstanding for operating and finance leases on December 31, 2022.

Manufacturing and service contract obligations primarily relate to manufacturing of inventory for our approved products, the majority of which are due in the next 12 months. See Note 15 to the Consolidated Financial Statements for these contractual obligations.

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 amount and timing of such obligations are unknown or uncertain. These potential obligations are further described in Note 8 to the Consolidated Financial Statements.

**Recent Accounting Pronouncements**

None.

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

*Interest Rate Risk*

Our exposure to market risk for changes in interest rates relates primarily to interest earned on our cash equivalents and marketable debt securities. 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, 2022, we had cash, cash equivalents, and marketable debt securities totaling $896.7 million, which included 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 the fair market value of our cash equivalents and marketable debt securities as of December 31, 2022. To date, we have not experienced a loss of principal on any of our investments and as of December 31, 2022, we did not record any allowance for credit loss from 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. Volatile market conditions arising from the COVID-19 pandemic, the macro-economic environment, inflation, or global political instability may result in significant changes in exchange rates, and in particular a weakening of foreign currencies relative to the U.S. dollar may negatively affect our revenue and operating income as expressed in U.S. dollars. An adverse movement in foreign exchange rates could have a material effect on payments made to foreign suppliers and payments related to license agreements. For the year ended December 31, 2022, a majority of our revenue, expenses, 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**

Management carried out an evaluation, under the supervision and with the participation of our Principal Executive Officer and Principal 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(e) and 15d-15(e) under the Securities Exchange Act of 1934, or the Exchange Act. Based on this evaluation, our Principal Executive Officer and Principal 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, 2022. 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 recognizes 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 applies 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, 2022 and has concluded that as of such date, our internal control over financial reporting was 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, 2022, 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, 2022, 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, 2022, 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 Ultragenyx Pharmaceutical Inc. as of December 31, 2022 and 2021, 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, 2022, and the related notes, and our report dated February 16, 2023 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 Mateo, California
February 16, 2023

**Item 9B. *Other Information***

None.

**Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections**

Not applicable.

## PART III

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

Except as set forth below, the information required by this Item is incorporated herein by reference to information in the proxy statement for our 2023 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, or the "2023 Proxy Statement", including under the headings "Nominees and Incumbent Directors," "Executive Officers," ""Board of Directors and Committees," and, as applicable, "Delinquent Section 16(a) Beneficial Ownership 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 website located at https://ir.ultragenyx.com/ under "Corporate Governance". 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 2023 Proxy Statement, including under the headings "Executive Compensation," "Director Compensation," and "Board of Directors and Committees"

**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 2023 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 2023 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 2023 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 | Form of Common Stock Certificate | S-1 | 11/8/2013 | 4.2 | |
| 4.2 | Form of Indenture | S-3 ASR | 2/12/2021 | 4.2 | |
| 4.3 | Description of Common Stock | 10-K | 2/14/2020 | 4.3 | |
| 10.1 | Open Market Sales Agreement, dated May 7, 2021, between Ultragenyx Pharmaceutical Inc. and Jefferies LLC | 8-K | 5/7/2021 | 1.1 | |
| 10.2* | Collaboration and License Agreement, effective as of August 29, 2013, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd. | S-1/A | 12/23/2013 | 10.1 | |
| 10.3 | Amendment No. 1 to Collaboration and License Agreement, effective as of August 24, 2015, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd. | 10-Q | 11/10/2015 | 10.2 | |
| 10.4 | 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 | |
| 10.5* | 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 | |
| 10.6* | 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 | |
| 10.7* | 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 | |
| 10.8* | 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 | |

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|---|---|---|---|---|
| 10.9* | 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 |
| 10.10* | 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 |
| 10.11* | Amendment No. 9 to Collaboration and License Agreement, effective December 23, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. | 10-K | 2/14/2020 | 10.10 |
| 10.12* | Amendment No. 10 to Collaboration and License Agreement, effective as of April 1, 2020, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. | 10-Q | 5/7/2020 | 10.2 |
| 10.13* | Amendment No. 11 to Collaboration and License Agreement, effective as of December 17, 2021 between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. | 10-K | 2/16/2022 | 10.13 |
| 10.14* | Amendment No. 12 to Collaboration and License Agreement, effective as of September 29, 2022, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. | 10-Q | 11/3/2022 | 10.1 |
| 10.15* | License Agreement, dated as of September 20, 2012, between Ultragenyx Pharmaceutical Inc. and Baylor Research Institute | 10-K | 2/12/2021 | 10.12 |
| 10.16* | Amendment to the License Agreement, dated as of March 22, 2013, between Ultragenyx Pharmaceutical Inc. and Baylor Research Institute | 10-K | 2/12/2021 | 10.13 |
| 10.17* | 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 |
| 10.18* | License Agreement, dated October 30, 2013, between Dimension Therapeutics, Inc. and REGENXBIO Inc. (f/k/a ReGenX Biosciences, LLC), as amended | 10-K | 2/21/2018 | 10.13 |
| 10.19* | Option and License Agreement, dated March 10, 2015, between Dimension Therapeutics, Inc. and REGENXBIO Inc. | 10-K | 2/21/2018 | 10.14 |
| 10.20* | First Amendment to Option and License Agreement, dated March 18, 2019, between REGENXBIO, Inc. and Ultragenyx Pharmaceutical Inc. (as assignee of Dimension Therapeutics, Inc.) | 10-Q | 5/7/2019 | 10.1 |
| 10.21* | Second Amendment to Option and License Agreement, dated December 17, 2021, between REGENXBIO, Inc. and Ultragenyx Pharmaceutical Inc. | 10-K | 2/16/2022 | 10.20 |
| 10.22* | Research, Collaboration and License Agreement, dated as of May 5, 2016, between Dimension Therapeutics, Inc. and The Trustees of the University of Pennsylvania, as amended | 10-K | 2/21/2018 | 10.16 |
| 10.23* | 3rd Amendment to Research, Collaboration and License Agreement, entered into as of October 30, 2017, between Dimension Therapeutics, Inc. and The Trustees of the University of Pennsylvania | 10-K | 2/21/2018 | 10.17 |

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|---|---|---|---|---|---|
| 10.24* | 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 | |
| 10.25* | Commercial Master Service Agreement – Drug Product, effective February 22, 2021, between Ultragenyx Pharmaceutical Inc. and BSP Pharmaceuticals S.p.A | | | | X |
| 10.26 | 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 | |
| 10.27* | Master Services Agreement, dated April 8, 2019, between Ultragenyx Pharmaceutical Inc. and Aenova Haupt Pharma Wolfratshausen GmbH | 10-K | 2/12/2021 | 10.24 | |
| 10.28* | Royalty Purchase Agreement, dated as of December 17, 2019, between Ultragenyx Pharmaceutical Inc. and RPI Finance Trust | 10-K | 2/14/2020 | 10.25 | |
| 10.29* | Royalty Purchase Agreement, dated as of July 14, 2022, by and among Rare Delaware Inc., Ultragenyx Pharmaceutical Inc. and OCM LS23 Holdings LP | 10-Q | 7/29/2022 | 10.1 | |
| 10.30* | Unit Purchase Agreement, dated as of July 15, 2022, by and among Ultragenyx Pharmaceutical Inc., GeneTx Biotherapeutics LLC, the Unitholders and Deborah A. Guagliardo | 10-Q | 7/29/2022 | 10.2 | |
| 10.31# | 2011 Equity Incentive Plan (including forms of Stock Option Grant Notice and Stock Option Agreement thereunder) | S-1 | 11/8/2013 | 10.11 | |
| 10.32# | Amendment to the 2011 Equity Incentive Plan | S-1 | 11/8/2013 | 10.12 | |
| 10.33# | 2014 Incentive Plan (as amended) | 10-K | 2/17/2017 | 10.20 | |
| 10.34# | Form of Incentive Stock Option Agreement | S-1/A | 1/17/2014 | 10.14 | |
| 10.35# | Form of Non Statutory Stock Option Agreement (Employees) | S-1/A | 1/17/2014 | 10.15 | |
| 10.36# | Form of Non Statutory Stock Option Agreement (Employees) (ex-U.S.) | 10-Q | 5/10/2016 | 10.3 | |
| 10.37# | Form of Restricted Stock Unit Agreement (Employees) | 10-Q | 5/10/2016 | 10.1 | |
| 10.38# | Form of Restricted Stock Unit Agreement (Employees)(ex-U.S.) | 10-Q | 5/10/2016 | 10.2 | |
| 10.39# | Form of Non-Statutory Stock Option Agreement (Annual Grant for Directors) | 10-Q | 8/3/2021 | 10.2 | |
| 10.40# | Form of Restricted Stock Unit Agreement (Annual Grant for Directors) | 10-Q | 8/3/2021 | 10.3 | |
| 10.41# | Form of Non-Statutory Stock Option Agreement (Grant for New Directors) | 10-Q | 8/3/2021 | 10.4 | |
| 10.42# | Form of Restricted Stock Unit Agreement (Grant for New Directors) | 10-Q | 8/3/2021 | 10.5 | |
| 10.43# | Form of Performance Stock Unit Agreement (2021) | 10-Q | 5/5/2021 | 10.1 | |
| 10.44# | Form of Performance Stock Unit Agreement (2022) | 10-Q | 5/6/2022 | 10.1 | |
| 10.45# | 2014 Employee Stock Purchase Plan (as amended) | 10-K | 2/17/2017 | 10.28 | |
| 10.46# | Corporate Bonus Plan | S-1/A | 1/17/2014 | 10.27 | |

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|---|---|---|---|---|
| 10.47# | Employment Inducement Plan | 10-K | 2/12/2021 | 10.43 |
| 10.48# | Form of Non Statutory Stock Option Agreement (Inducement Plan) | 10-K | 2/12/2021 | 10.44 |
| 10.49# | Form of Non Statutory Stock Option Agreement (Inducement Plan) (ex-US) | 10-K | 2/12/2021 | 10.45 |
| 10.50# | Form of Restricted Stock Unit Agreement (Inducement Plan) | 10-K | 2/12/2021 | 10.46 |
| 10.51# | Form of Restricted Stock Unit Agreement (Inducement Plan) (ex-US) | 10-K | 2/12/2021 | 10.47 |
| 10.52# | Ultragenyx Pharmaceutical Inc. Deferred Compensation Plan | 10-Q | 8/3/2021 | 10.1 |
| 10.53# | Amendment No. 1 to the Ultragenyx Pharmaceutical Inc. Deferred Compensation Plan | 10-Q | 11/3/2021 | 10.1 |
| 10.54# | 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 |
| 10.55# | Amendment No. 1 to Executive Employment Agreement, dated August 8, 2014, between Ultragenyx Pharmaceutical Inc. and Emil D. Kakkis, M.D., Ph.D. | 10-Q | 8/11/2014 | 10.2 |
| 10.56# | Amendment No. 2, dated September 13, 2022, to Executive Employment Agreement between Ultragenyx Pharmaceutical Inc. and Emil D. Kakkis, M.D., Ph.D. | 10-Q | 11/3/2022 | 10.2 |
| 10.57# | Offer Letter, dated as of October 31, 2011, between Ultragenyx Pharmaceutical Inc. and Thomas Kassberg | S-1 | 11/8/2013 | 10.19 |
| 10.58# | Amendment No. 1 to Offer Letter, dated as of August 8, 2014, between Ultragenyx Pharmaceutical Inc. and Thomas Kassberg | 10-Q | 8/11/2014 | 10.3 |
| 10.59# | Amendment No. 2, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Thomas Kassberg | 10-Q | 11/3/2022 | 10.5 |
| 10.60# | Offer Letter, dated as of April 26, 2016, between Ultragenyx Pharmaceutical Inc. and Karah Parschauer | 10-Q | 8/9/2016 | 10.3 |
| 10.61# | Amendment, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Karah Parschauer | 10-Q | 11/3/2022 | 10.6 |
| 10.62# | Offer Letter, dated as of February 20, 2015, between Ultragenyx Pharmaceutical Inc. and Dennis Huang | 10-K | 2/17/2017 | 10.36 |
| 10.63# | Amendment, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Dennis Huang | 10-Q | 11/3/2022 | 10.7 |
| 10.64# | Offer Letter, dated as of June 11, 2015, between Ultragenyx Pharmaceutical Inc. and John R. Pinion II | 10-K | 2/17/2017 | 10.37 |
| 10.65# | Amendment, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and John R. Pinion II | 10-Q | 11/3/2022 | 10.9 |
| 10.66# | Offer Letter, dated as of January 15, 2018, between Ultragenyx Pharmaceutical Inc. and Camille Bedrosian, M.D. | 10-K | 2/21/2018 | 10.46 |

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| 10.67# | Amendment, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Camille Bedrosian, M.D. | 10-Q | 11/3/2022 | 10.3 |
| 10.68# | Offer Letter, dated May 16, 2017, between Ultragenyx Pharmaceutical Inc. and Erik Harris | 10-Q | 8/2/2019 | 10.4 |
| 10.69# | 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 |
| 10.70# | 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 |
| 10.71# | Amendment No. 3, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Erik Harris | 10-Q | 11/3/2022 | 10.8 |
| 10.72# | Form of Indemnification Agreement | 10-K | 3/24/2014 | 10.23 |
| 10.73 | Standard Lease, dated as of July 5, 2011, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc. | S-1 | 11/8/2013 | 10.22 |
| 10.74 | 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 |
| 10.75 | 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 |
| 10.76 | Addendum #3 to Standard Lease, effective as of February 12, 2014, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc. | 8-K | 2/25/2014 | 10.1 |
| 10.77 | Addendum #4 to Standard Lease, effective as of March 9, 2015, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc. | 8-K | 3/13/2015 | 10.1 |
| 10.78 | Addendum #5 to Standard Lease, effective as of April 7, 2015, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc. | 10-K | 2/26/2016 | 10.38 |
| 10.79 | Addendum #6 to Standard Lease, effective as of April 29, 2019, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc. | 10-Q | 8/2/2019 | 10.3 |
| 10.80 | Lease Agreement, dated as of December 8, 2015, between Marina Boulevard Property, LLC and Ultragenyx Pharmaceutical Inc. | 10-K | 2/26/2016 | 10.43 |
| 10.81 | Indenture of Lease, dated March 11, 2014, between Dimension Therapeutics, Inc. and Rivertech Associates II, LLC | 10-K | 2/21/2018 | 10.64 |
| 10.82 | Second Lease Amendment, dated April 28, 2017, to the Lease between Dimension Therapeutics, Inc. and Rivertech Associates II, LLC | 10-K | 2/21/2018 | 10.65 |
| 10.83 | Third Lease Amendment, dated December 31, 2018, to the Lease between Ultragenyx Pharmaceutical Inc. and Rivertech Associates II, LLC | 10-K | 2/20/2019 | 10.66 |

| | | | | | |
|---|---|---|---|---|---|
| 10.84 | Lease Agreement, dated November 2, 2015, between Dimension Therapeutics, Inc. and ARE-MA Region No. 20, LLC, and Consent to Assignment to Ultragenyx Pharmaceutical Inc. | 10-K | 2/21/2018 | 10.66 | |
| 10.85 | 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 | |
| 10.86 | Second Amendment to Lease Agreement, dated July 1, 2018, between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No. 20, LLC | 10-Q | 8/3/2018 | 10.3 | |
| 10.87 | Third Amendment to the Lease Agreement, dated July 29, 2019, between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No., LLC. | 10-Q | 7/30/2020 | 10.2 | |
| 10.88 | Amended and Restated Fourth Amendment, dated August 4, 2020, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No., LLC. | 10-Q | 10/27/2020 | 10.5 | |
| 10.89 | Lease Agreement, dated December 15, 2019, between Ultragenyx Pharmaceutical Inc. and ARE-San Francisco No. 17, LLC. | 10-K | 2/12/2021 | 10.81 | |
| 10.90 | First Amendment, dated September 20, 2020, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and ARE-San Francisco No. 17, LLC. | 10-K | 2/12/2021 | 10.82 | |
| 10.91 | Second Amendment, dated October 21, 2020, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and ARE-San Francisco No. 17, LLC. | 10-K | 2/12/2021 | 10.83 | |
| 10.92 | Third Amendment, dated July 27, 2022, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and ARE-San Francisco No. 17, LLC | | | | X |
| 10.93 | Office Lease, dated April 19, 2019, between Ultragenyx Pharmaceutical Inc. and Woburn MCB II, LLC | 10-K | 2/14/2020 | 10.70 | |
| 10.94 | Commercial Lease, dated July 2, 2018, between Ultragenyx Pharmaceutical Inc. and 32 Leveroni LLC | 10-K | 2/14/2020 | 10.71 | |
| 10.95 | Lease, dated August 18, 2022, between Ultragenyx Pharmaceutical Inc. and Brickbottom I QOZB L.P. | | | | 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 Principal Executive Officer and Principal 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 |
| 32.1§ | Certification by the Principal Executive Officer and Principal 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 this Annual Report on Form 10-K, formatted in Inline XBRL | |

* Certain identified information has been omitted by means of marking such information with asterisks in reliance on Item 601(b)(10)(iv) of Regulation S-K because it is both (i) not material and (ii) the type that the registrant treats as private or confidential.

# 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*

*(Principal Executive Officer and Principal Financial Officer)*

Date: February 16, 2023

## 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., 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<br>Emil D. Kakkis, M.D., Ph.D. | President and Chief Executive Officer and Director<br>(Principal Executive Officer and Principal Financial Officer) | February 16, 2023 |
| /s/ Theodore A. Huizenga<br>Theodore A. Huizenga | Senior Vice President and Chief Accounting Officer<br>(Principal Accounting Officer) | February 16, 2023 |
| /s/ Daniel G. Welch<br>Daniel G. Welch | Chairman of the Board | February 16, 2023 |
| /s/ Deborah Dunsire<br>Deborah Dunsire, M.D. | Director | February 16, 2023 |
| /s/ Lars Ekman<br>Lars Ekman, M.D., Ph.D. | Director | February 16, 2023 |
| /s/ Matthew K. Fust<br>Matthew K. Fust | Director | February 16, 2023 |
| /s/ Michael Narachi<br>Michael Narachi | Director | February 16, 2023 |
| /s/ Corsee D. Sanders<br>Corsee D. Sanders, Ph.D. | Director | February 16, 2023 |
| /s/ Amrit Ray, M.D.<br>Amrit Ray, M.D. | Director | February 16, 2023 |
| /s/ Shehnaaz Suliman<br>Shehnaaz Suliman, M.D. | Director | February 16, 2023 |

**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, 2022 and 2021, 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, 2022, 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 at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, 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 16, 2023 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 U.S. 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 included 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 Matter**

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter 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 matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

***Liabilities for sales of future royalties***

| | |
|---|---|
| *Description of the Matter* | As discussed in Note 10, the Company has entered into two royalty purchase agreements, under which the Company sold its rights to receive royalty payments arising from the net sales of Crysvita in the European and North American markets in exchange for $320 million and $500 million, respectively. The proceeds from each transaction were recorded as liabilities that are being amortized using the effective interest method over the estimated lives of the respective arrangements. In order to determine the amortization of the liabilities, the Company is required to estimate the total amount of future royalty payments to be paid to the respective counterparty, subject to the capped amount, over the life of the arrangement. The Company estimates an imputed interest on the unamortized portion of the liability and records non-cash interest expense relating to the transaction.<br><br>Auditing the Company’s liabilities related to the sale of future royalties was complex due to the subjective judgments required to forecast the expected royalty payments subject to each agreement. Specifically, the forecasted revenues of Crysvita involve significant estimation uncertainty given the limited historical Crysvita sales data. |

| | |
|---|---|
| *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 accounting for the liabilities related to the sale of future royalties, including controls over the Company's estimates of projected sales of Crysvita in the European and North American markets.<br><br>To test management's estimates of the future royalties and the imputed effective interest rates, we performed audit procedures that included, among others, evaluating the reasonableness of management's assumptions related to the treatable patient populations, estimated pricing and reimbursement, and the rate of adoption. We compared the significant assumptions with historical trends of actual sales, analyst expectations and performed sensitivity analyses of estimated future royalties to evaluate the changes in the future royalties on the implied effective interest rates. |

/s/ Ernst & Young LLP

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

San Mateo, California
February 16, 2023

**ULTRAGENYX PHARMACEUTICAL INC.**

**CONSOLIDATED BALANCE SHEETS**
**(In thousands, except share and per share amounts)**

| | December 31, | |
|---|---|---|
| | **2022** | **2021** |
| **ASSETS** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 132,944 | $ 307,584 |
| Marketable debt securities | 614,818 | 432,612 |
| Accounts receivable, net | 40,445 | 28,432 |
| Inventory | 26,766 | 16,231 |
| Prepaid expenses and other current assets | 68,926 | 71,745 |
| Total current assets | 883,899 | 856,604 |
| Property, plant, and equipment, net | 259,726 | 141,247 |
| Equity investments | 5,531 | 34,925 |
| Marketable debt securities | 148,970 | 258,933 |
| Right-of-use assets | 25,961 | 34,936 |
| Intangible assets, net | 160,105 | 130,788 |
| Goodwill | 44,406 | 44,406 |
| Other assets | 16,846 | 20,558 |
| Total assets | $ 1,545,444 | $ 1,522,397 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY** | | |
| Current liabilities: | | |
| Accounts payable | $ 43,274 | $ 17,138 |
| Accrued liabilities | 204,678 | 145,555 |
| Contract liabilities | 1,479 | 7,609 |
| Lease liabilities | 11,779 | 11,066 |
| Total current liabilities | 261,210 | 181,368 |
| Contract liabilities | — | 1,467 |
| Lease liabilities | 19,814 | 30,904 |
| Deferred tax liabilities | 31,667 | 33,306 |
| Liabilities for sales of future royalties | 875,439 | 351,786 |
| Other liabilities | 4,820 | 1,005 |
| Total liabilities | 1,192,950 | 599,836 |
| Commitments and contingencies (Notes 9 and 15) | | |
| Stockholders' equity: | | |
| Preferred stock, par value of $0.001 per share—25,000,000 shares authorized; nil outstanding as of December 31, 2022 and December 31, 2021 | — | — |
| Common stock, par value of $0.001 per share—250,000,000 shares authorized; 70,197,297 and 69,344,998 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively | 70 | 69 |
| Additional paid-in capital | 3,140,019 | 2,997,497 |
| Accumulated other comprehensive loss | (6,573) | (1,404) |
| Accumulated deficit | (2,781,022) | (2,073,601) |
| Total stockholders' equity | 352,494 | 922,561 |
| Total liabilities and stockholders' equity | $ 1,545,444 | $ 1,522,397 |

See accompanying notes.

**ULTRAGENYX PHARMACEUTICAL INC.**

**CONSOLIDATED STATEMENTS OF OPERATIONS**
**(In thousands, except share and per share amounts)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2022** | **2021** | **2020** |
| Revenues: | | | |
| Collaboration and license | $ 222,710 | $ 256,438 | $ 219,315 |
| Product sales | 118,927 | 77,017 | 38,720 |
| Non-cash collaboration royalty revenue | 21,692 | 17,951 | 12,995 |
| Total revenues | 363,329 | 351,406 | 271,030 |
| Operating expenses: | | | |
| Cost of sales | 28,320 | 16,008 | 6,129 |
| Research and development | 705,789 | 497,153 | 412,084 |
| Selling, general and administrative | 278,139 | 219,982 | 182,933 |
| Total operating expenses | 1,012,248 | 733,143 | 601,146 |
| Loss from operations | (648,919) | (381,737) | (330,116) |
| Interest income | 11,074 | 1,928 | 7,038 |
| Change in fair value of equity investments | (19,299) | (42,063) | 170,403 |
| Non-cash interest expense on liabilities for sales of future royalties | (43,015) | (29,422) | (33,291) |
| Other income (expense) | (1,566) | (1,687) | 607 |
| Loss before income taxes | (701,725) | (452,981) | (185,359) |
| Provision for income taxes | (5,696) | (1,044) | (1,207) |
| Net loss | $ (707,421) | $ (454,025) | $ (186,566) |
| Net loss per share, basic and diluted | $ (10.12) | $ (6.70) | $ (3.07) |
| Weighted-average shares used in computing net loss per share, basic and diluted | 69,914,225 | 67,795,540 | 60,845,550 |

See accompanying notes.

**ULTRAGENYX PHARMACEUTICAL INC.**

**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**
**(In thousands)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2022** | **2021** | **2020** |
| Net loss | $ (707,421) | $ (454,025) | $ (186,566) |
| Other comprehensive income (loss): | | | |
| Foreign currency translation adjustments | (724) | (550) | 735 |
| Unrealized gain (loss) on available-for-sale securities | (4,445) | (1,543) | 101 |
| Other comprehensive income (loss): | (5,169) | (2,093) | 836 |
| Total comprehensive loss | $ (712,590) | $ (456,118) | $ (185,730) |

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, 2019 | 57,838,220 | $ 58 | $ 2,086,863 | $ (147) | $ (1,433,010) | $ 653,764 |
| Issuance of common stock in connection with underwritten public offering, net of issuance costs | 5,111,110 | 5 | 435,551 | — | — | 435,556 |
| Issuance of common stock in connection with license agreement, net of issuance costs | 1,243,913 | 1 | 55,267 | — | — | 55,268 |
| Issuance of common stock in connection with at-the-market offering, net of issuance costs | 283,333 | — | 20,391 | — | — | 20,391 |
| Stock-based compensation | — | — | 85,833 | — | — | 85,833 |
| Issuance of common stock upon exercise of warrants and under equity plan awards, net of tax | 2,341,944 | 3 | 89,290 | — | — | 89,293 |
| Other comprehensive income | — | — | — | 836 | — | 836 |
| Net loss | — | — | — | — | (186,566) | (186,566) |
| Balance as of December 31, 2020 | 66,818,520 | 67 | 2,773,195 | 689 | (1,619,576) | 1,154,375 |
| Issuance of common stock in connection with at-the-market offering, net of issuance costs | 1,050,372 | 1 | 78,942 | — | — | 78,943 |
| Stock-based compensation | — | — | 105,260 | — | — | 105,260 |
| Issuance of common stock under equity plan awards, net of tax | 1,476,106 | 1 | 40,100 | — | — | 40,101 |
| Other comprehensive loss | — | — | — | (2,093) | — | (2,093) |
| Net loss | — | — | — | — | (454,025) | (454,025) |
| Balance as of December 31, 2021 | 69,344,998 | 69 | 2,997,497 | (1,404) | (2,073,601) | 922,561 |
| Stock-based compensation | — | — | 131,710 | — | — | 131,710 |
| Issuance of common stock under equity plan awards, net of tax | 852,299 | 1 | 10,812 | — | — | 10,813 |
| Other comprehensive loss | — | — | — | (5,169) | — | (5,169) |
| Net loss | — | — | — | — | (707,421) | (707,421) |
| Balance as of December 31, 2022 | 70,197,297 | $ 70 | $ 3,140,019 | $ (6,573) | $ (2,781,022) | $ 352,494 |

See accompanying notes.

**ULTRAGENYX PHARMACEUTICAL INC.**

**CONSOLIDATED STATEMENTS OF CASH FLOWS**
**(In thousands)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2022** | **2021** | **2020** |
| **Operating activities:** | | | |
| Net loss | $ (707,421) | $ (454,025) | $ (186,566) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Stock-based compensation | 130,377 | 104,952 | 85,735 |
| Acquired in-process research and development | 75,033 | — | — |
| Amortization of premium (discount) on marketable debt securities, net | 2,699 | 6,606 | 848 |
| Depreciation and amortization | 18,220 | 13,239 | 12,261 |
| Change in fair value of equity investments | 19,299 | 42,063 | (170,403) |
| Non-cash collaboration royalty revenue | (21,692) | (17,951) | (12,995) |
| Non-cash interest expense on liabilities for sales of future royalties | 43,015 | 29,422 | 33,291 |
| Other | (230) | 235 | 946 |
| Changes in operating assets and liabilities: | | | |
| Accounts receivable | (12,068) | (5,432) | 9,840 |
| Inventory | (9,701) | (3,117) | (1,346) |
| Prepaid expenses and other assets | 3,798 | (29,508) | 2,748 |
| Accounts payable, accrued, and other liabilities | 87,442 | 32,313 | 26,853 |
| Contract liabilities, net | (7,597) | (57,492) | 66,568 |
| Deferred tax liabilities | (1,639) | — | — |
| Net cash used in operating activities | (380,465) | (338,695) | (132,220) |
| **Investing activities:** | | | |
| Purchase of property, plant, and equipment | (116,123) | (73,093) | (43,905) |
| Acquisition, net of cash acquired | (75,025) | — | — |
| Purchase of marketable debt securities | (614,735) | (1,012,187) | (813,237) |
| Purchase of equity investments | — | — | (37,062) |
| Proceeds from sale of marketable debt securities | 84,275 | 92,896 | 50,990 |
| Proceeds from sale of equity investments | 10,094 | 79,843 | 79,842 |
| Proceeds from maturities of marketable debt securities | 450,706 | 718,111 | 589,806 |
| Payment for intangible asset | (30,000) | — | — |
| Other | (844) | (942) | (5,555) |
| Net cash used in investing activities | (291,652) | (195,372) | (179,121) |
| **Financing activities:** | | | |
| Proceeds from the sale of future royalties, net | 490,950 | — | — |
| Proceeds from the issuance of common stock in connection with underwritten public offerings, net | — | — | 435,556 |
| Proceeds from the issuance of common stock in connection with the license agreement, net | — | — | 55,268 |
| Proceeds from the issuance of common stock in connection with at-the-market offering, net | — | 78,943 | 20,391 |
| Proceeds from the issuance of common stock from exercise of warrants and equity plan awards, net | 10,813 | 40,101 | 89,293 |
| Other | (555) | (492) | (236) |
| Net cash provided by financing activities | 501,208 | 118,552 | 600,272 |
| Effect of exchange rate changes on cash | (1,075) | (1,194) | 1,119 |
| Net (decrease) increase in cash, cash equivalents, and restricted cash | (171,984) | (416,709) | 290,050 |
| Cash, cash equivalents, and restricted cash at beginning of year | 309,585 | 726,294 | 436,244 |
| Cash, cash equivalents, and restricted cash at end of year | $ 137,601 | $ 309,585 | $ 726,294 |

See accompanying notes.

**ULTRAGENYX PHARMACEUTICAL INC.**

**CONSOLIDATED STATEMENTS OF CASH FLOWS**
**(In thousands)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2022** | **2021** | **2020** |
| **Supplemental disclosures of non-cash investing and financing information:** | | | |
| Acquired lease liabilities arising from obtaining right-of-use assets | $ 1,168 | $ 3,142 | $ 18,775 |
| Stock-based compensation capitalized into ending inventory | $ 2,340 | $ 1,453 | $ 1,304 |
| Costs of property, plant and equipment included in accounts payable, accrued, and other liabilities | $ 17,963 | $ 18,993 | $ 8,515 |
| Non-cash interest expense on liabilities for sales of future royalties capitalized during the year into ending property, plant and equipment | $ 11,380 | $ 4,650 | $ — |

See accompanying notes.

## 1. Organization and Basis of Presentation

Ultragenyx Pharmaceutical Inc., or the Company, is a biopharmaceutical company incorporated in Delaware.

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 operates as one reportable segment and has four commercially approved products.

Crysvita® (burosumab) is approved in the United States, or U.S., the European Union, or EU, and certain other regions for the treatment of X-linked hypophosphatemia, or XLH, in adult and pediatric patients one year of age and older. Crysvita is also approved in the U.S. and certain other regions for the treatment of fibroblast growth factor 23, or FGF23,-related hypophosphatemia in tumor-induced osteomalacia, or TIO, associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older.

Mepsevii® (vestronidase alfa) is approved in the U.S., the EU and certain other regions, as the first medicine for the treatment of children and adults with mucopolysaccharidosis VII, or MPS VII, also known as Sly syndrome.

Dojolvi® (triheptanoin) is approved in the U.S. and certain other regions for the treatment of pediatric and adult patients severely affected by long-chain fatty acid oxidation disorders, or LC-FAOD.

Evkeeza® (evinacumab) is approved in the U.S. and the European Economic Area, or EEA, for the treatment of homozygous familial hypercholesterolemia, or HoFH. In January 2022, the Company licensed exclusive rights from Regeneron Pharmaceuticals, or Regeneron, to commercialize Evkeeza® (evinacumab) outside of the U.S.

In addition to the approved products, the Company has the following ongoing clinical development programs:

- UX111 (formerly ABO-102) is an AAV9 gene therapy product candidate for the treatment of patients with Sanfilippo syndrome type A, or MPS IIIA, a rare lysosomal storage disease. In May 2022, the Company announced an exclusive license agreement with Abeona Therapeutics Inc., or Abeona, for UX111 whereby the Company assumed responsibility for the UX111 program, as further described in Note 8;
- DTX401 is an adeno-associated virus 8, or AAV8, gene therapy product candidate for the treatment of patients with glycogen storage disease type Ia, or GSDIa;
- DTX301 is an AAV8 gene therapy product candidate in development for the treatment of patients with ornithine transcarbamylase, or OTC deficiency, the most common urea cycle disorder;
- UX143 (setrusumab), which is subject to the Company's collaboration agreement with Mereo BioPharma 3, or Mereo, is a fully human monoclonal antibody that inhibits sclerostin, a protein that acts on a key bone-signaling pathway and inhibits the activity of bone-forming cells for the treatment of patients with osteogenesis imperfect, or OI;
- GTX-102 is an antisense oligonucleotide, or ASO, which the Company is developing through GeneTx Biotherapeutics LLC, or GeneTx, for the treatment of Angelman syndrome, a debilitating and rare neurogenetic disorder caused by loss-of-function of the maternally inherited allele of the UBE3A gene. In July 2022, the Company executed its option to acquire GeneTx as further described in Note 7;
- UX701 is an adeno-associated virus 9, or AAV9, gene therapy designed to deliver stable expression of a truncated version of the ATP7B copper transporter following a single intravenous infusion to improve copper distribution and excretion from the body and reverse pathological findings of Wilson liver disease; and
- UX053 is a messenger RNA, or mRNA, product candidate designed for the treatment of patients with Glycogen Storage Disease Type III, or GSDIII, a disease caused by a glycogen debranching enzyme, or AGL, deficiency that results in glycogen accumulation in the liver and muscle.

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. Management recognizes that the Company will likely need to raise additional capital to fully implement its business plans. Through December 31, 2022, the Company has relied primarily on its sale of equity securities, its revenues from commercial products, its sale of future royalties, and strategic collaboration arrangements, to finance its operations.

The Company expects it will need 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 would 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 its 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, or 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, stock-based compensation, revenue recognition, and the liabilities for sales of future royalties. 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 and the gene therapy building construction project.

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 Statements of Cash Flows (in thousands):

| | December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Cash and cash equivalents | $132,944 | $ 307,584 | $ 713,526 |
| Restricted cash included in prepaid expenses and other current assets | 862 | — | 10,847 |
| Restricted cash included in other assets | 3,795 | 2,001 | 1,921 |
| Total cash, cash equivalents, and restricted cash shown in the statements of cash flows | $137,601 | $ 309,585 | $ 726,294 |

### Marketable Debt Securities

All marketable debt securities 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 current marketable debt securities and investments with a maturity of greater than one year from the balance sheet date are reported as non-current marketable debt securities. 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.

### Equity Investments

The Company records investments in equity securities, other than equity method investments, at fair market value, if the fair value is readily determinable. Equity securities with no readily determinable fair values are recorded using the measurement alternative of cost adjusted for observable price changes in orderly transactions for identical or similar investments of the same issuer less impairment, if any. Investments in equity securities are recorded in Equity investments on the Company's Consolidated

Balance Sheets. Unrealized gains and losses are reported in Change in fair value of equity investments on the Company's Consolidated Statements of Operations. The Company regularly reviews its non-marketable equity securities for indicators of impairment.

**Concentration of Credit Risk, Credit Losses, 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 Consolidated Balance Sheets.

For trade receivables and other instruments, the Company uses a new forward-looking expected loss model that generally results in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses, the losses are recognized as allowances rather than as reductions in the amortized cost of the securities.

The Company is exposed to credit losses primarily through receivables from customers and collaborators and through its available-for-sale debt securities. For trade receivables and other instruments, the Company uses a forward-looking expected loss model that generally results in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses, the losses are recognized as allowances rather than as reductions in the amortized cost of the securities.

The Company's expected loss allowance methodology for the receivables is developed using historical collection experience, current and future economic market conditions, a review of the current aging status and financial condition of the entities. Specific allowance amounts are established to record the appropriate allowance for customers that have a higher probability of default. Balances are written off when determined to be uncollectible. The Company's expected loss allowance methodology for the debt securities is developed by reviewing the extent of the unrealized loss, the size, term, geographical location, and industry of the issuer, the issuers' credit ratings and any changes in those ratings, as well as reviewing current and future economic market conditions and the issuers' current status and financial condition. There was no allowance for losses on available-for-sale debt securities which were attributable to credit risk for the years ended December 31, 2022 and 2021.

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, Plant, and Equipment**

Property, plant, 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. Interest costs incurred during the construction of major capital projects are capitalized until the underlying asset is ready to be placed in service, at which point the interest costs are amortized as depreciation expense over the life of the underlying asset. Maintenance and repairs are charged to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation or amortization are removed from the balance sheet and the resulting gain or loss, if any, is reflected in operations.

The useful lives of property, plant, and equipment are as follows:

| | |
|---|---|
| Research and development equipment | 5 years |
| Furniture and office equipment | 5 years |
| Computer equipment and software | 3-5 years |
| Land | Not applicable |
| Leasehold improvements | Shorter of lease term or estimated useful life |

**Intangible Assets**

Finite-lived intangibles consist of contractual payments made for certain milestones achieved with collaboration partners. The contractual payments are recorded as intangible assets and are amortized over their estimated useful lives. The Company reviews its definite-lived intangible assets when events or circumstances may indicate that the carrying value of these assets is not recoverable and exceeds their fair value. The Company measures fair value based on the estimated future undiscounted cash flows associated with these assets in addition to other assumptions and projections that the Company deems to be reasonable and supportable.

Indefinite-lived intangibles consist of acquired in-process research and development, or IPR&D. 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. When development of the project 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 Company tests its 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 an intangible 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 to date.

**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 obtaining information from 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, or 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. The Company records its share of collaboration revenue, net of transfer pricing related to net sales in the period in which such sales occur, if the Company is considered as an agent in the arrangement. The Company is considered an agent when the collaboration partner controls the product before transfer to the customers and has the ability to direct the use of and obtain substantially all of the remaining benefits from the product. 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 Statements 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.

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 Company also records 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.

The Company sold the right to receive certain royalty payments from net sales of Crysvita in certain territories to RPI Finance Trust, or RPI, an affiliate of Royalty Pharma, and to OCM LS23 Holdings LP, an investment vehicle for Ontario Municipal Employees Retirement System, or OMERS, as further described in "Note 10. Liabilities for Sales of Future Royalties". The Company records the royalty revenue from the net sales of Crysvita in the applicable territories on a prospective basis as non-cash royalty revenue in the Consolidated Statements of Operations over the term of the applicable arrangement.

The terms of the Company's collaboration and license 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, or* 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 obligations and recognizes revenue by measuring the progress towards complete satisfaction of the performance obligations using input measures.

*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. The Company's estimates of government mandated rebates, chargebacks, estimated product returns, and other deductions depends on the identification of key customer contract terms and conditions, as well as estimates of sales volumes to different classes of payors. If actual results vary, the Company may need to adjust these estimates, which could have a material effect on earnings in the period of the adjustment.

**Leases**

Lease agreements are evaluated to determine whether an arrangement is or contains a lease in accordance with ASC 842, *Leases*. 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. The Company has elected to not separate lease and non-lease components. 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, performance stock options, or PSOs, restricted stock units, or RSUs, and performance stock units, or 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). PSOs and 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 PSOs and 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 the acquisition of Dimension Therapeutics, Inc., or Dimension, 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.

## 3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, accounts 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 and U.S. Government treasury bills are classified as Level 1. Level 2 assets consist primarily of corporate bonds, asset backed securities, commercial paper, U.S. Government Treasury and agency securities, and debt securities in government-sponsored entities 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 its equity investments in Arcturus Therapeutics Holdings Inc., or Arcturus, and Solid Biosciences, Inc., or Solid, by using the quoted market prices, which are Level 1 fair value measurements.

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

| | December 31, 2022 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| **Financial Assets:** | | | | |
| Money market funds | $ 102,847 | $ — | $ — | $ 102,847 |
| Certificates of deposits and time deposits | — | 25,972 | — | 25,972 |
| Corporate bonds | — | 427,598 | — | 427,598 |
| Commercial paper | — | 135,393 | — | 135,393 |
| Asset-backed securities | — | 11,980 | — | 11,980 |
| U.S. Government Treasury and agency securities | 27,645 | 129,345 | — | 156,990 |
| Debt securities in government-sponsored entities | — | 15,855 | — | 15,855 |
| Investment in Solid common stock | 2,807 | — | — | 2,807 |
| Other | — | 4,575 | — | 4,575 |
| Total | $ 133,299 | $ 750,718 | $ — | $ 884,017 |

| | December 31, 2021 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| **Financial Assets:** | | | | |
| Money market funds | $ 266,765 | $ — | $ — | $ 266,765 |
| Certificates of deposits and time deposits | — | 16,000 | — | 16,000 |
| Corporate bonds | — | 349,691 | — | 349,691 |
| Commercial paper | — | 187,624 | — | 187,624 |
| Asset-backed securities | — | 41,245 | — | 41,245 |
| U.S. Government Treasury and agency securities | — | 87,435 | — | 87,435 |
| Debt securities in government-sponsored entities | — | 19,549 | — | 19,549 |
| Investments in Arcturus and Solid common stock | 32,200 | — | — | 32,200 |
| Other | — | 942 | — | 942 |
| Total | $ 298,965 | $ 702,486 | $ — | $ 1,001,451 |

## 4. Balance Sheet Components

### Cash Equivalents and Marketable Debt Securities

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

| | December 31, 2022 | | | |
|---|---|---|---|---|
| | | Gross Unrealized | | |
| | Amortized Cost | Gains | Losses | Estimated Fair Value |
| Money market funds | $ 102,847 | $ — | $ — | $ 102,847 |
| Certificates of deposit and time deposits | 25,972 | — | — | 25,972 |
| Corporate bonds | 432,211 | 87 | (4,700) | 427,598 |
| Commercial paper | 135,393 | — | — | 135,393 |
| Asset-backed securities | 12,002 | — | (22) | 11,980 |
| U.S. Government Treasury and agency securities | 157,933 | 320 | (1,263) | 156,990 |
| Debt securities in government-sponsored entities | 16,005 | — | (150) | 15,855 |
| Total | $ 882,363 | $ 407 | $ (6,135) | $ 876,635 |

| | December 31, 2021 | | | |
|---|---|---|---|---|
| | | Gross Unrealized | | |
| | Amortized Cost | Gains | Losses | Estimated Fair Value |
| Money market funds | $ 266,765 | $ — | $ — | $ 266,765 |
| Certificates of deposit and time deposits | 16,000 | — | — | 16,000 |
| Corporate bonds | 350,667 | 3 | (979) | 349,691 |
| Commercial paper | 187,624 | — | — | 187,624 |
| Asset-backed securities | 41,282 | 1 | (38) | 41,245 |
| U.S. Government Treasury and agency securities | 87,642 | 1 | (208) | 87,435 |
| Debt securities in government-sponsored entities | 19,612 | — | (63) | 19,549 |
| Total | $ 969,592 | $ 5 | $ (1,288) | $ 968,309 |

At December 31, 2022, the remaining contractual maturities of available-for-sale securities were less than three years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented. The unrealized losses on the Company's investments in marketable debt securities were caused by increases in market yields on these investments. The contractual terms of these investments do not permit the issuers to settle the securities at a price less than the par value. Accordingly, it is expected that the securities will not be settled at a price less than the amortized cost basis of these investments. The Company does not intend to sell the investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost basis.

**Inventory**

Inventory consists of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Work-in-process | $ 17,486 | $ 10,504 |
| Finished goods | 9,280 | 5,727 |
| Total | $ 26,766 | $ 16,231 |

**Property, Plant, and Equipment, net**

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

| | December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Leasehold improvements | $ 43,941 | $ 44,081 |
| Research and development equipment | 50,291 | 38,661 |
| Furniture and office equipment | 5,540 | 5,413 |
| Computer equipment and software | 13,876 | 10,238 |
| Land | 16,619 | 15,487 |
| Construction-in-progress | 189,448 | 76,849 |
| Other | 3,392 | 556 |
| Property, plant, and equipment, gross | 323,107 | 191,285 |
| Less: accumulated depreciation | (63,381) | (50,038) |
| Property, plant, and equipment, net | $ 259,726 | $ 141,247 |

Depreciation expense for the years ended December 31, 2022, 2021, and 2020 was $15.0 million, $12.9 million and $12.1 million, respectively. Amortization of leasehold improvements and software is included in depreciation expense. The construction-in-progress balance primarily relates to the construction costs for the gene therapy manufacturing plant in Bedford, Massachusetts.

**Accrued Liabilities**

Accrued liabilities consists of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Research, clinical study, and manufacturing expenses | $ 73,558 | $ 40,880 |
| Payroll and related expenses | 78,938 | 62,591 |
| Other | 52,182 | 42,084 |
| Total | $ 204,678 | $ 145,555 |

## 5. Intangible Assets, net

*Indefinite-lived Intangibles*

The Company has IPR&D assets of $129.0 million as of December 31, 2022 and 2021. 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.

*Finite-lived Intangibles*

Subsequent to the FDA approval of Dojolvi for the treatment of LC-FAOD in 2020, the Company recorded $4.8 million for the attainment of various development and commercial milestones as finite-lived intangible assets which are amortized over a weighted-average useful life of 5.7 years.

In January 2022, the Company announced a collaboration with Regeneron to commercialize Evkeeza for HoFH outside of the U.S. Upon closing of the transaction in January 2022, the Company paid Regeneron a $30.0 million upfront payment. As the upfront payment was related to the Company's usage of intellectual property related to Evkeeza for HoFH, the upfront payment was recorded as an intangible asset, which is amortized over its useful life of 10.5 years.

The Company's intangible assets were as follows:

| | December 31, 2022 | | | |
|---|---|---|---|---|
| | Gross Carrying Amount | Weighted-Average Life (Years) | Accumulated Amortization | Net Carrying Amount |
| Indefinite-lived intangibles | $ 129,000 | — | $ — | $ 129,000 |
| Finite-lived intangibles | 34,775 | 9.9 | $ (3,670) | $ 31,105 |
| Total intangible assets | $ 163,775 | — | $ (3,670) | $ 160,105 |

| | December 31, 2021 | | | |
|---|---|---|---|---|
| | Gross Carrying Amount | Weighted-Average Life (Years) | Accumulated Amortization | Net Carrying Amount |
| Indefinite-lived intangibles | $ 129,000 | — | $ — | $ 129,000 |
| Finite-lived intangibles | 2,275 | 7.0 | $ (487) | $ 1,788 |
| Total intangible assets | $ 131,275 | — | $ (487) | $ 130,788 |

The Company recorded costs of sales of $3.2 million, $0.3 million and $0.2 million for the years ended December 31, 2022, 2021, and 2020, respectively, related to the amortization of the intangible assets.

The expected amortization of the intangible assets, as of December 31, 2022, for each of the next five years and thereafter is as follows:

| | |
|---|---|
| 2023 | $ 3,738 |
| 2024 | 3,738 |
| 2025 | 3,738 |
| 2026 | 3,738 |
| 2027 | 3,297 |
| Thereafter | 12,856 |
| Total | $ 31,105 |

## 6. Revenue

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Collaboration and license revenue: | | | |
| Crysvita collaboration revenue in profit-share territory | $ 215,024 | $ 171,198 | $ 128,597 |
| Crysvita royalty revenue in European territory | — | 244 | 1,498 |
| Daiichi Sankyo | 7,686 | 84,996 | 89,220 |
| Total collaboration and license revenue | 222,710 | 256,438 | 219,315 |
| Product sales: | | | |
| Crysvita | 42,678 | 21,422 | 10,350 |
| Mepsevii | 20,637 | 16,035 | 15,342 |
| Dojolvi | 55,612 | 39,560 | 13,028 |
| Total product sales | 118,927 | 77,017 | 38,720 |
| Crysvita non-cash collaboration royalty revenue | 21,692 | 17,951 | 12,995 |
| Total revenues | $ 363,329 | $ 351,406 | $ 271,030 |

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| North America | $ 281,088 | $ 301,110 | $ 237,666 |
| Europe | 36,369 | 26,660 | 21,318 |
| Latin America | 44,711 | 23,636 | 12,046 |
| Japan | 1,161 | — | — |
| Total revenues | $ 363,329 | $ 351,406 | $ 271,030 |

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Balance of product sales reserve at beginning of year | $ 7,181 | $ 3,913 | $ 1,818 |
| Provisions | 13,525 | 9,586 | 5,763 |
| Payments | (9,613) | (6,120) | (2,785) |
| Adjustments | 394 | (198) | (883) |
| Balance of product sales reserve at end of year | $ 11,487 | $ 7,181 | $ 3,913 |

The following table presents changes in the contract assets (liabilities) for the years ended December 31, 2022 and 2021 (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Balance of contract liabilities at beginning of period | $ 9,076 | $ 66,568 |
| Additions | 89 | 27,504 |
| Deductions | (7,686) | (84,996) |
| Balance of contract liabilities at end of period, net | $ 1,479 | $ 9,076 |

See Note 8 for additional details on contract liabilities activities.

The Company's largest accounts receivable balance was from a collaboration partner and was 68% and 71% of the total accounts receivable balance as of December 31, 2022 and 2021, respectively.

## 7. GeneTx Acquisition

In August 2019, the Company entered into a Program Agreement and a Unitholder Option Agreement with GeneTx Biotherapeutics LLC, or GeneTx, to collaborate on the development of GeneTx's GTX-102, an 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, which was exercisable any time prior to 30 days following FDA acceptance of the IND for GTX-102. Pursuant to the agreement, upon acceptance of the IND, which occurred in January 2020, the Company elected to extend the option period by paying an option extension payment of $25.0 million during the quarter ended March 31, 2020, which was recorded as an in-process research and development expense. In April 2022, the parties entered into an amendment to the Unitholder Option Agreement, or the Amendment, which provided the Company with an additional, earlier option to acquire GeneTx for an option exercise price of $75.0 million based on the earlier of receipt of interim data in the Phase 1/2 study or a specified date, such option, the Interim Option.

During the exclusive option period, GeneTx was responsible for conducting the program based on the development plan agreed upon between the parties and, subject to the terms in the Program Agreement, had the decision-making authority on all matters in connection with the research, development, manufacturing and regulatory activities with respect to the Program.

In July 2022, the Company exercised the Interim Option to acquire GeneTx and entered into a Unit Purchase Agreement, or the Purchase Agreement, pursuant to which the Company purchased all the outstanding units of GeneTx. In accordance with the terms of the Purchase Agreement, the Company paid the option exercise price of $75.0 million and an additional $15.6 million to acquire the outstanding cash of GeneTx, and adjustments for working capital and transaction expenses of $0.6 million, for a total purchase consideration of $91.2 million. Additionally, the Company may make payments of up to $190.0 million upon the achievement of certain milestones, including up to $30.0 million in milestone payments upon achievement of the earlier of initiation of a Phase 3 clinical study or product approvals in Canada and the U.K., up to $85.0 million in additional regulatory approval milestones for the achievement of U.S. and EU product approvals, and up to $75.0 million in commercial milestone payments based on annual worldwide net product sales. In addition, the Company will also pay tiered mid- to high single-digit percentage royalties based on licensed product annual net sales. If the Company receives and resells an FDA priority review voucher, or PRV, in connection with a new drug application approval, GeneTx is entitled to receive a portion of proceeds from the sale or a cash payment from the Company if the Company choses to retain the PRV.

The transaction was accounted as an asset acquisition, as substantially all of the fair value of the gross assets acquired was concentrated in a single identifiable in-process research and development intangible asset. Prior to the achievement of certain development and regulatory milestones, the acquired in-process research and development intangible asset has not yet reached technological feasibility and has no alternative future use. Accordingly, the Company recorded the acquisition price of $75.0 million, net of cash and working capital acquired, as in-process research and development expense during the year ended December 31, 2022.

## 8. License and Research Agreements

### Kyowa Kirin Co., Ltd.

In August 2013, the Company entered into a collaboration and license agreement with Kyowa Kirin Co., Ltd., or KKC (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 U.S. 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 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. In April 2023, which is the transition date for the profit-share 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.

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 the 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 a 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. In April 2023, commercialization responsibilities for Crysvita in the profit-share territory will transition to KKC and KKC will be responsible for the commercialization of Crysvita in the territory at and after April 2023. Thereafter, the Company will be entitled to receive a tiered double-digit revenue share from the mid-20% range up to a maximum rate of 30%.

In September 2022, the Company entered into an amendment to the collaboration agreement which clarified the scope of increased participation by KKC in support of the Company's commercial activities prior to April 2023 and granted the Company the right to continue to support KKC in commercial field activities in the U.S. through April 2024, subject to the limitations and conditions set forth in the amendment. As a result, KKC will continue to support the Company's commercial field and marketing efforts through a cost share arrangement through April 2024, subject to the limits and conditions set forth in the amendment. After April 2024, the Company's rights to promote Crysvita in the U.S. will be limited to medical geneticists and the Company will solely bear its expenses related to the promotion of Crysvita in the profit-share territory.

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.

In July 2022, the Company sold to OMERS its right to receive 30% of the future royalty payments due to the Company based on net sales of Crysvita in the U.S. and Canada, subject to a cap, beginning in April 2023, as further described in Note 10.

*Royalty Revenue Related to Sales in the European Territory*

KKC has the commercial responsibility for Crysvita in the European territory. In December 2019, the Company sold its right to receive royalty payments based on sales in the European territory to Royalty Pharma, effective January 1, 2020, as further described in "Note 10. Liabilities for Sales of Future Royalties." Prior to the Company's sale of the royalty, the Company received a royalty of up to 10% on net sales in the European territory, which was recognized as the underlying sales occur. Beginning in 2020, the Company records the royalty revenue as non-cash royalty revenues. During the years ended December 31, 2021 and 2020, there was a change in estimate of the revenue reserves related to sales made prior to January 1, 2020, as a result of which, the Company recorded $0.2 million and $1.5 million, respectively, as royalty revenue in the European territory.

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Company's share of revenue in profit-share territory | $ 215,024 | $ 171,198 | $ 128,597 |
| Royalty revenue in European territory | — | 244 | 1,498 |
| Non-cash royalty revenue in European territory | 21,692 | 17,951 | 12,995 |
| Total | $ 236,716 | $ 189,393 | $ 143,090 |

*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. The Company recorded product sales of $42.7 million, $21.4 million, and $10.4 million for the years ended December 31, 2022, 2021, and 2020, respectively, net of estimated product returns and other deductions. 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 its 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, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Research and development | $ 15,974 | $ 21,657 | $ 21,476 |
| Selling, general and administrative | 37,217 | 32,629 | 25,186 |
| Total | $ 53,191 | $ 54,286 | $ 46,662 |

*Collaboration Receivable and Payable*

The Company had accounts receivable from KKC in the amount of $27.5 million and $20.2 million from profit-share revenue and royalties and other receivables recorded in prepaid expenses and other current assets of $6.4 million and $16.0 million and accrued liabilities of $3.1 million and $2.3 million from commercial and development activity reimbursements, as of December 31, 2022 and 2021, respectively.

**Saint Louis University**

In November 2010, the Company entered into a license agreement with Saint Louis University, or 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**

In September 2012, the Company entered into a license agreement with Baylor Research Institute, or BRI. Under the terms of this license agreement, as amended, BRI exclusively licensed to the Company its territories for certain intellectual property related to Dojolvi (triheptanoin) for the treatment of LC-FAOD.

For the years ended December 31, 2022, 2021, and 2020, the Company recorded $2.5 million, nil and $2.0 million, respectively, for the attainment of various development and commercial milestones as finite-lived intangible assets. The Company is obligated to make additional future payments of up to $7.5 million contingent upon attainment of various development and commercial milestones. Additionally, the Company is paying BRI a mid- single-digit royalty on net sales of the licensed product in the licensed territories.

**REGENXBIO, Inc.**

The Company has a license agreement with REGENXBIO, Inc., or 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 to treat Wilson disease and CDKL5 deficiency. For each disease indication, the Company is obligated to pay an annual maintenance fee of $0.1 million and 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.

In March 2020, the Company entered into a license agreement with REGENX, for an exclusive, sublicensable, worldwide license to REGENX's NAV AAV8 and AAV9 vectors for the development and commercialization of gene therapy treatments for a rare metabolic disorder. In return for these rights, the Company made an upfront payment of $7.0 million, which was recorded as an in-process research and development expense during the year ended December 31, 2020. The Company will pay certain annual fees of $0.1 million, milestone payments of up to $14.0 million, and royalties on any net sales of products incorporating the licensed intellectual property that range from a high single-digit to low double-digit royalty.

**Bayer HealthCare LLC**

The Company previously had a collaboration and license agreement with Bayer Healthcare LLC, or Bayer, to research, develop and commercialize AAV gene therapy products for the treatment of hemophilia A, or DTX 201. Under this agreement, Bayer had been granted an exclusive license to develop and commercialize one or more novel gene therapies for hemophilia A.

In October 2022, the Collaboration and License Agreement for DTX201 with Bayer was terminated and all licensed rights to DTX201 have reverted back to the Company. The Company also obtained rights to all necessary data and information to further develop DTX201 or another hemophilia A program through a royalty-free, worldwide, sublicensable, perpetual license.

**University of Pennsylvania**

The Company has a research, collaboration, and license agreement with University of Pennsylvania School of Medicine, or 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. The Company is also obligated to make milestone payments of up to $25.0 million per approved product if certain commercial milestones are achieved, as well as low to mid- single-digit royalties on net sales of each licensed product.

**Arcturus Therapeutics Holdings Inc.**

In October 2015, the Company entered into a Research Collaboration and License Agreement with Arcturus Therapeutics Holdings Inc., or Arcturus, to collaborate on the research and development of therapies for select rare diseases. Arcturus was responsible for conducting certain research services, funded by the Company, and the Company was responsible for development and commercialization costs.

On a product-by-product basis, the Company is obligated to make development and regulatory milestone payments of up to $24.5 million, and commercial milestone payments of up to $45.0 million if certain milestones are achieved. For the year ended December 31, 2021, the Company achieved a $1.0 million development milestone related to UX053, which was paid with a corresponding credit received from Arcturus for prior research and collaboration activities. The Company is also obligated to pay Arcturus royalties on any net sales of products incorporating the licensed intellectual property that may range from a mid- single-digit to low double-digit percentage. Pursuant to the agreement, the Company incurred nil, nil, and $0.4 million for the years ended December 31, 2022, 2021, and 2020, respectively, in research and development expense for the funding of certain research services received from Arcturus.

In June 2019, the Company entered into an Equity Purchase Agreement and an amendment to the Research Collaboration and License Agreement, or 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 under the License Agreement, Arcturus common stock, and an option to purchase an additional 600,000 shares of Arcturus' common stock at

$16.00 per share. In May 2020, the Company exercised its option to purchase 600,000 shares of Arcturus common stock for a total purchase price of $9.6 million.

During the years ended December 31, 2022 and 2021, the Company sold 500,000 shares and 1,700,000 shares of Arcturus common stock, at a weighted-average price of $20.39 and $47.44, respectively. As of December 31, 2022 and 2021, the Company held nil and 500,000 shares, respectively, of Arcturus common stock.

The Company's investment in Arcturus was accounted at fair value, as the fair value was readily determinable. All remaining shares of Arcturus held by the Company were sold during the year ended December 31, 2022.

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

| | Arcturus Common Stock |
|---|---|
| December 31, 2020 | $ 95,436 |
| Change in fair value | 2,912 |
| Sale of shares | (79,843) |
| December 31, 2021 | 18,505 |
| Change in fair value | (8,411) |
| Sale of shares | (10,094) |
| December 31, 2022 | $ — |

**Daiichi Sankyo**

In March 2020, the Company executed a License and Technology Access Agreement, or the License Agreement, with Daiichi Sankyo Co., Ltd., or Daiichi Sankyo. Pursuant to the License Agreement, the Company granted Daiichi Sankyo a non-exclusive license to intellectual property, including know-how and patent applications, with respect to its Pinnacle PCL™ producer cell line platform, or Pinnacle PCL Platform, and HEK293 transient transfection manufacturing technology platforms for AAV-based gene therapy products. The Company retains the exclusive right to use the manufacturing technology for its current target indications and additional indications identified now and in the future. The Company will provide certain technical assistance and technology transfer services during the technology transfer period of three years to enable Daiichi Sankyo to use the technologies for its internal gene therapy programs. Daiichi Sankyo has an option to extend the technology transfer period including know-how improvements by two additional one-year periods by paying a fixed amount for each additional year. Daiichi Sankyo will be responsible for the manufacturing, development, and commercialization of products manufactured with the licensed technology; however, the Company has the option to co-develop and co-commercialize rare disease products at the IND stage. The Company may also provide strategic consultation to Daiichi Sankyo on the development of both AAV-based gene therapy products and other products for rare diseases.

Under the terms of the License Agreement, Daiichi Sankyo made an upfront payment of $125.0 million and an additional $25.0 million payment upon completion of the technology transfer of the Pinnacle PCL Platform and HEK293 platform. Daiichi Sankyo reimbursed the Company for all costs associated with the transfer of the manufacturing technology and will pay single-digit royalties on net sales of products manufactured in either system.

The Company also entered into a Stock Purchase Agreement, or SPA, with Daiichi Sankyo, pursuant to which Daiichi Sankyo purchased 1,243,913 shares of the Company's common stock in exchange for $75.0 million in cash during the first quarter of 2020. The fair market value of the common stock issued to Daiichi Sankyo was $55.3 million based on the stock price of $44.43 per share on the date of issuance, resulting in a $19.7 million premium on the SPA. Daiichi Sankyo is also subject to a three-year standstill and restrictions on sale of the shares (subject to customary exceptions or release).

In June 2020, the Company executed a subsequent license agreement, or the Sublicense Agreement, with Daiichi Sankyo for transfer of certain technology in consideration for an upfront payment of $8.0 million and annual maintenance fees, milestone payments, and royalties on any net sales of products incorporating the licensed intellectual property.

The License Agreement, the Sublicense Agreement, and the SPA are being accounted for as one arrangement because they were entered into at or near the same time and negotiated in contemplation of one another. The Company evaluated the License Agreement and the Sublicense Agreement under ASC 606 and determined that the performance obligations under the agreements are (i) intellectual property with respect to its Pinnacle PCL Platform and HEK293 transient transfection manufacturing technology platform together with the initial technical assistance and technology transfer services, which was completed in the first quarter of 2022, and (ii) the transfer of any know-how and improvements after the completion of the initial technology transfer through the end of the three year technology transfer period ending March 2023.

As of December 31, 2022, the Company has determined that the total transaction price of the License Agreement was $183.3 million which was comprised of the $19.7 million premium from the SPA, the $125.0 million upfront payment, the $25.0 million in unconstrained milestone payments, $8.0 million from the Sublicense Agreement, and the $5.6 million estimated reimbursement amount for delivering the license and technology services. Total revenue recognized under the license agreement through December 31, 2022 was $181.9 million.

The Company allocated the total transaction price to the two performance obligations on a relative stand-alone selling price basis. Revenue allocated to the intellectual property and the technology transfer services was recognized over an initial period which was completed during the first quarter of 2022.Progress toward complete satisfaction of the individual performance obligation used an input measure. Revenue for know-how and improvements after the completion of technology transfer is recognized on a straight-line basis over the remaining technology transfer period, which ends in March 2023, as it is expected that Daiichi Sankyo will receive and consume the benefits consistently throughout the period. Royalties from commercial sales will be accounted for as revenue upon achievement of such sales, assuming all other revenue recognition criteria are met.

The Company recognized $7.7 million, $85.0 million, and $89.2 million respectively, for the years ended December 31, 2022, 2021, and 2020 in revenue related to this arrangement. As of December 31, 2022 and 2021, the Company had recorded contract liabilities of $1.5 million and $9.1 million and an accounts receivable related to the above agreements of nil and $0.1 million, respectively.

**Mereo**

In December 2020, the Company entered into a License and Collaboration Agreement with Mereo BioPharma 3, or Mereo, to collaborate on the development of setrusumab. Under the terms of the agreement, the Company will lead future global development of setrusumab in both pediatric and adult patients with OI. The Company was granted an exclusive license to develop and commercialize setrusumab in the U.S., Turkey, and the rest of the world, excluding the EEA, U.K., and Switzerland, or the Mereo territory, where Mereo retains commercial rights. Each party will be responsible for post-marketing commitments and commercial supply in their respective territories.

Upon the closing of the transaction in January 2021, the Company made a payment of $50.0 million to Mereo and will be required to make payments of up to $254.0 million upon the achievement of certain clinical, regulatory, and commercial milestones. The Company will pay for all global development costs as well as tiered double-digit percentage royalties to Mereo on net sales in the U.S., Turkey, and the rest of the world (excluding the Mereo Territory), and Mereo will pay the Company a fixed double-digit percentage royalty on net sales in the Mereo Territory.

Although Mereo is a variable interest entity, the Company is not the primary beneficiary as it does not have the power to direct the activities that would most significantly impact the economic performance of Mereo. Prior to the achievement of certain development milestones, all consideration paid to Mereo represents rights to potential future benefits associated with Mereo's in-process research and development activities, which have not reached technological feasibility and have no alternative future use. Accordingly, for the three months ended March 31, 2021, the Company recorded the upfront payment of $50.0 million as in-process research and development expense.

**Regeneron**

In January 2022, the Company announced a collaboration with Regeneron Pharmaceuticals, or Regeneron, to commercialize Evkeeza for HoFH outside of the U.S. Evkeeza is approved in the U.S., where it is marketed by Regeneron, and in the EU and U.K. as a first-in-class therapy for use together with diet and other low-density lipoprotein-cholesterol-lowering therapies to treat adults and adolescents aged 12 years and older with HoFH. Pursuant to the terms of the agreement, the Company received the rights to develop, commercialize and distribute the product for HoFH in countries outside of the U.S. The Company is obligated to pay up to $63.0 million in future milestone payments, contingent upon the achievement of certain regulatory and sales milestones. The Company may share in certain costs for global trials led by Regeneron and also received the right to opt into other potential indications, including a right to negotiate a separate agreement with Regeneron to collaborate on the Regeneron's investigational antibody for the treatment of fibrodysplasia ossificans progressiva, or FOP, which expired in July 2022.

The collaboration agreement is within the scope of ASC 808 which provides guidance on the presentation and disclosure of collaborative arrangements. As the Company would be the principal in future sale transactions with the customer, the Company will recognize product sales and cost of sales in the period the related sales occur and the related revenue recognition criteria are met.

Under the collaboration agreement, Regeneron will supply the product and will charge the Company a transfer price from the low 20% range up to 40% on net sales, which will be recognized as cost of sales in the Company's Statement of Operations.

Upon the closing of the transaction in January 2022, the Company paid Regeneron a $30.0 million upfront payment. As the upfront payment was related to the Company's usage of intellectual property related to Evkeeza for HoFH, the upfront payment was recorded as an intangible asset, which is amortized over its useful life of 10.5 years.

The Company recorded costs of sales of $2.9 million, for the year ended December 31, 2022, related to the amortization of the intangible asset. Further, the Company reimbursed Regeneron for certain costs of $7.3 million that was recorded as research and development expense for the year ended December 31, 2022. No sales of Evkeeza were recorded for the year ended December 31, 2022.

**Abeona**

In May 2022, the Company announced an exclusive License Agreement for the AAV gene therapy for UX111 with Abeona for the treatment of MPS IIIA. Under the terms of the agreement, the Company assumed responsibility for the UX111 program and in return, Abeona is eligible to receive tiered royalties of up to 10% on net sales and commercial milestone payments of up to $30.0 million following regulatory approval of the product. Additionally, the Company entered into an Assignment and Assumption Agreement with Abeona to transfer and assign to the Company the exclusive license agreement between Nationwide Children's Hospital, or NCH, and Abeona for certain rights related to UX111. Under this agreement, NCH is eligible to receive from the Company up to $1.0 million in development and regulatory milestones as well as royalties in the low single-digits of net sales.

The Company is obligated to pay Abeona certain prior development costs and other transition costs related to UX111. Prior to product regulatory approval, all consideration paid to Abeona represents rights to potential future benefits associated with Abeona's in-process research and development activities, which have not reached technological feasibility and have no alternative future use. Accordingly, the value of the acquired intellectual property rights and clinical inventory as well as prior development costs and transition costs of $3.1 million were recorded as research and development expense for the year ended December 31, 2022.

**Solid Biosciences, Inc.**

In October 2020, the Company entered into a strategic Collaboration and License Agreement with Solid Biosciences Inc., or Solid, and received an exclusive license for any pharmaceutical product that expresses Solid's proprietary microdystrophin construct from AAV8 and variants thereof in clade E for use in the treatment of Duchenne muscular dystrophy and other diseases resulting from lack of functional dystrophin, including Becker muscular dystrophy. The Company is collaborating to develop products that combine Solid's differentiated microdystrophin construct, the Company's Pinnacle PCL Platform, and the Company's AAV8 variants. Solid is providing development support and was granted an exclusive option to co-invest in products the Company develops for profit-share participation in certain territories. On a product-by-product basis, the Company is obligated to make development milestone payments of up to $25.0 million, regulatory milestone payments of up to $65.0 million, and commercial milestone payments of up to $165.0 million, if such milestones are achieved, as well as royalties on any net sales of products incorporating the licensed intellectual property that range from a low to mid-double-digit percentage. The royalty rate changes to mid- to high double-digit percentage if Solid decides to co-invest in the product.

The Company also entered into a Stock Purchase Agreement and the Investor Agreement with Solid, pursuant to which, the Company purchased 7,825,797 shares of Solid's common stock for an aggregate purchase price of $40.0 million. In October 2022, Solid announced a 1 for 15 reverse stock split. After the split, the Company holds 521,719 shares in Solid. The Company's investment in Solid is being accounted at fair value, as the fair value is readily determinable. The Company recorded the common stock investment at $26.8 million on the transaction date, which was based on the quoted market price on the closing date.

Although Solid is a variable interest entity, the Company is not the primary beneficiary as it does not have the power to direct the activities that would most significantly impact the economic performance of Solid. Prior to the achievement of certain development milestones, all consideration paid to Solid represents rights to potential future benefits associated with Solid's in-process research and development activities, which have not reached technological feasibility and have no alternative future use. Accordingly, the remaining $13.2 million of the total $40.0 million paid as consideration was attributed to the license rights obtained and was recorded as in-process research and development expense during the year ended December 31, 2020.

The changes in the fair value of the Company's investment in Solid's common stock were as follows (in thousands):

| | Solid Common Stock |
|---|---|
| December 31, 2020 | $ 59,320 |
| Change in fair value | (45,625) |
| December 31, 2021 | 13,695 |
| Change in fair value | (10,888) |
| December 31, 2022 | $ 2,807 |

## 9. Leases

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Operating lease expense | $ 11,775 | $ 11,209 | $ 10,164 |
| Variable lease expense | 4,785 | 4,142 | 3,298 |
| Financing: | | | |
| Amortization | 343 | 310 | 158 |
| Interest expense | 37 | 58 | 40 |
| Total | $ 16,940 | $ 15,719 | $ 13,660 |

Cash paid for amounts included in the measurement of operating lease liabilities for the years ended December 31, 2022, 2021, and 2020 was $13.1 million, $11.8 million, and $10.3 million, respectively, and was included in net cash used in operating activities in the Consolidated Statements of Cash Flows.

The following table summarizes maturities of lease liabilities and the reconciliation of lease liabilities as of December 31, 2022:

| Year Ending December 31, | Operating | Financing | Total |
|---|---|---|---|
| 2023 | $ 13,244 | $ 187 | $ 13,431 |
| 2024 | 11,372 | — | 11,372 |
| 2025 | 6,530 | — | 6,530 |
| 2026 | 2,964 | — | 2,964 |
| 2027 | 446 | — | 446 |
| Thereafter | 376 | — | 376 |
| Total future lease payments | 34,932 | 187 | 35,119 |
| Less: Amount representing interest | (3,522) | (4) | (3,526) |
| Present value of future lease payments | 31,410 | 183 | 31,593 |
| Less: Lease liabilities, current | (11,596) | (183) | (11,779) |
| Lease liabilities, non-current | $ 19,814 | $ — | $ 19,814 |

The table above excludes $23.4 million of legally binding minimum lease payments for a lease that was executed during the year ended December 31, 2022, but whose term had not commenced. The Company is also obligated to pay $9.9 million of fit-out costs related to this lease.

Lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. For the years ended December 31, 2022 and 2021, the weighted-average remaining operating lease terms were 3.01 years and 3.84 years, respectively, the weighted-average remaining financing lease terms were 2.81 years and 3.88 years, respectively, the weighted-average discount rates used to determine the lease liability for operating leases were 6.72% and 6.64%, respectively, and the weighted-average discount rates used to determine the lease liability for finance leases were 5.13% and 5.44% respectively.

## 10. Liabilities for Sales of Future Royalties

In December 2019, the Company entered into a Royalty Purchase Agreement with RPI. 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 EU, the U.K., and Switzerland under the terms of the Company's Collaboration and License Agreement with KKC dated August 29, 2013, as amended, or the KKC Collaboration Agreement. 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, or when aggregate royalty payments received by RPI are equal to $800.0 million.

In July 2022, the Company entered into a Royalty Purchase Agreement with OMERS. Pursuant to the agreement, OMERS paid $500.0 million to the Company in consideration for the right to receive 30% of the future royalty payments due to the Company from KKC based on net sales of Crysvita in the U.S. and Canada under the terms of the KKC Collaboration Agreement. The calculation of royalty payments to OMERS will be based on net sales of Crysvita beginning in April 2023 and will expire upon the earlier of the date on which aggregate payments received by OMERS equals $725.0 million or the date the final royalty payment is made to the Company under the KKC Collaboration Agreement.

Proceeds from these transactions were recorded as liabilities for sales of future royalties on the Consolidated Balance Sheets. Upon inception of the respective arrangements, the Company recorded $320.0 million and $500.0 million, net of transaction costs of $5.8 million and $9.1 million for RPI and OMERS, respectively, using the effective interest method over the estimated life of the applicable arrangement. In order to determine the amortization of the liabilities, the Company is required to estimate the total amount of future royalty payments to be received by the Company and paid to RPI and OMERS, subject to the capped amount, over the life of the arrangements. The excess of future estimated royalty payments (subject to the capped amount), over the $314.2 million and $491.0 million, respectively, of net proceeds, is recorded as non-cash interest expense over the life of the arrangements. Consequently, the Company estimates an imputed interest on the unamortized portion of the liabilities and records interest expense relating to the transactions. The Company records the royalty revenue arising from the net sales of Crysvita in the applicable territories as non-cash royalty revenue in the Consolidated Statements of Operations over the term of the arrangements.

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 liabilities and the effective interest rate. The Company's effective annual interest rate was approximately 9.3% and 8.4%, for RPI and OMERS, respectively, as of December 31, 2022.

There are a number of factors that could materially affect the amount and timing of royalty payments from KKC in the applicable 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, delays or disruptions related to the COVID-19 pandemic, macroeconomic and inflationary pressures, the introduction of competing products, pricing for reimbursement in various 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, or USD, while significant portions of the underlying sales of Crysvita are made in currencies other than USD, and other events or circumstances that could result in reduced royalty payments from 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 the relevant territories 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 arrangements.

The following table shows the activity within the liability account (in thousands):

| | Liabilities for Sales of Future Royalties | | |
|---|---|---|---|
| | RPI | OMERS | Total |
| December 31, 2020 | $ 335,665 | $ — | $ 335,665 |
| Non-cash collaboration royalty revenue | (17,951) | — | (17,951) |
| Non-cash interest expense | 34,072 | — | 34,072 |
| December 31, 2021 | 351,786 | — | 351,786 |
| Net proceeds from sale of future royalties | — | 490,950 | 490,950 |
| Non-cash collaboration royalty revenue | (21,692) | — | (21,692) |
| Non-cash interest expense | 35,095 | 19,300 | 54,395 |
| December 31, 2022 | $ 365,189 | $ 510,250 | $ 875,439 |

## 11. Equity

### At-the-Market Offerings

In May 2021, the Company entered into an Open Market Sale Agreement with Jefferies LLC, or Jefferies, pursuant to which the Company may offer and sell shares of the Company's common stock having an aggregate offering proceeds up to $350.0 million, from time to time, in ATM offerings through Jefferies. As of December 31, 2022, the Company has sold 1,050,372 shares under the arrangement resulting in net proceeds of approximately $78.9 million. No shares were sold under the arrangement for the year ended December 31, 2022.

### Underwritten Public Offering

In October 2020, the Company completed an underwritten public offering in which 5,111,110 shares of common stock were sold, which included 666,666 shares purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of $90.00 per share. The total proceeds that the Company received from the offering were approximately $435.6 million, net of underwriting discounts and commissions.

## 12. Stock-Based Awards

### Equity Plan Awards

In 2011, the Company adopted the 2011 Equity Incentive Plan, or 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, or 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. In February 2021, the Company adopted the Employment Inducement Plan, or the Inducement Plan, with a maximum of 500,000 shares available for grant under the Inducement Plan. Under the terms of the 2014 Plan and Inducement 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 and Inducement 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. Typically, 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 of December 31, 2022, an aggregate of 14,211,103 shares of common stock have been authorized for issuance under the 2011 Plan, the 2014 Plan, and the Inducement Plan.

**Stock Option Activity**

The following table summarizes activity under the Company's stock option 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, 2021 | 6,198,205 | $ 75.96 | 6.81 | $ 112,242 |
| Options granted | 2,293,950 | 64.88 | | |
| Options exercised | (130,865) | 47.70 | | |
| Options cancelled | (587,923) | 84.06 | | |
| Outstanding — December 31, 2022 | 7,773,367 | $ 72.56 | 6.60 | $ 8,476 |
| Vested and exercisable — December 31, 2022 | 4,577,580 | $ 70.89 | 5.14 | $ 7,658 |
| Vested and expected to vest — December 31, 2022 | 7,471,015 | $ 72.50 | 6.51 | $ 8,371 |

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, 2022, 2021, and 2020 was $2.6 million, $38.3 million, and $56.9 million, respectively. Cash received from the exercise of options was $6.2 million, $36.6 million, and $88.1 million for the years ended December 31, 2022, 2021, and 2020, respectively.

The weighted-average estimated fair value of stock options granted was $34.77, $70.84, and $35.22 per share of the Company's common stock during the years ended December 31, 2022, 2021, and 2020, respectively. The total estimated grant date fair value of options vested during the years ended December 31, 2022, 2021, and 2020 was $58.7 million, $48.1 million, and $45.4 million, respectively.

**Performance Stock Options**

The following table summarizes activity under the Company's Performance Stock Option, or PSO, plans and related information:

| | PSOs Outstanding | | | |
|---|---|---|---|---|
| | Number of Options | Weighted-Average Exercise Price | Weighted-Average Remaining Contractual Term (Years) | Aggregate Intrinsic Value |
| Outstanding — December 31, 2021 | — | $ — | — | $ — |
| PSOs granted | 1,827,449 | 67.37 | | |
| PSOs cancelled | (202,850) | 67.37 | | |
| Outstanding — December 31, 2022 | 1,624,599 | $ 67.37 | 4.14 | $ — |
| Vested and exercisable — December 31, 2022 | - | $ — | — | $ — |
| Vested and expected to vest — December 31, 2022 | 1,081,597 | $ 67.37 | 4.14 | $ — |

During the year ended December 31, 2022, PSOs were granted to certain nonexecutive employees. PSOs are subject to vest only if specified operational milestones are achieved and the employees' continued service with the Company. The Company uses the Black-Scholes method to calculate the fair value at the grant date and is recognizing stock-based compensation expense for the PSOs that are expected to vest. Stock-based compensation for PSOs is recognized over the service period, beginning in the period the Company determines it is probable that a milestone will be achieved. Forfeitures of PSOs are recognized as they occur. The Company reassesses the probability of the performance condition at each reporting period and adjusts the compensation cost based on the probability assessment. As of December 31, 2022, certain operational milestones were deemed probable of achievement. The aggregate intrinsic values of PSOs outstanding, vested and exercisable, and vested and expected to vest were calculated as the difference between the exercise price of the PSOs and the fair value of the Company's common stock. No PSOs vested or were exercised during the year ended December 31, 2022. The weighted-average estimated fair value of PSOs granted was $28.76 during the year ended December 31, 2022.

**Restricted Stock Units**

The following table summarizes activity under the Company's Restricted Stock Units, or RSU, plans and related information:

| | RSUs Outstanding | |
|---|---|---|
| | Number of Shares | Weighted- Average Grant Date Fair Value |
| Unvested — December 31, 2021 | 1,672,625 | $ 87.48 |
| RSUs granted | 1,347,125 | 63.22 |
| RSUs vested | (591,837) | 79.59 |
| RSUs cancelled | (298,760) | 81.84 |
| Unvested — December 31, 2022 | 2,129,153 | $ 75.11 |

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 RSUs vested during the years ended December 31, 2022, 2021, and 2020 was $47.1 million, $35.5 million, and $27.2 million, respectively. The aggregate intrinsic value of the shares of the RSUs vested during the years ended December 31, 2022, 2021, and 2020 was $37.8 million, $69.9 million, and $29.5 million, respectively.

**Performance Stock Units**

The following table summarizes activity under the Company's Performance Stock Units, or PSUs, from the 2014 Plan and related information:

| | PSUs Outstanding | |
|---|---|---|
| | Number of Shares | Weighted- Average Grant Date Fair Value |
| Unvested — December 31, 2021 | 93,892 | $ 123.46 |
| PSUs granted | 166,730 | 75.90 |
| PSUs vested | (28,990) | 56.08 |
| PSUs cancelled | (22,402) | 93.61 |
| Unvested — December 31, 2022 | 209,230 | $ 98.09 |

The fair value of the PSUs is determined on the grant date based on the fair value of the Company's common stock, except for certain PSUs with a market vesting condition, for which fair value is estimated using a Monte Carlo simulation model. 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, including both performance conditions and market conditions. As of December 31, 2022, the specified criteria were deemed probable of achievement or already achieved. Stock-based compensation for 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 PSUs vested during the years ended December 31, 2022, 2021, and 2020 was $1.6 million, $9.2 million, and $10.3 million, respectively, with an aggregate intrinsic value of the shares of $2.0 million, $18.9 million and $14.4 million, respectively.

**Employee Stock Purchase Plan**

In January 2014, the Company adopted the 2014 Employee Stock Purchase Plan, or 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, 2022, the Company issued 112,974 shares of common stock under the ESPP. As of December 31, 2022, an aggregate of 4,585,921 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, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Cost of sales | $ 902 | $ 871 | $ 827 |
| Research and development | 74,464 | 59,097 | 47,949 |
| Selling, general and administrative | 55,002 | 45,011 | 36,959 |
| Total stock-based compensation expense | $ 130,368 | $ 104,979 | $ 85,735 |

Stock-based compensation of $2.2 million, $1.7 million, and $1.2 million was capitalized into inventory for the years ended December 31, 2022, 2021, and 2020, respectively. Capitalized stock-based compensation is recognized as cost of sales when the related product is sold. As of December 31, 2022, the total unrecognized compensation expense related to unvested equity awards, net of estimated forfeitures, was $229.4 million, which the Company expects to recognize over an estimated weighted-average period of 2.28 years. In determining the estimated fair value of the stock options, PSOs 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.

Strike price for options awards and PSOs is equal to the closing market value of our common stock on the date of grant.

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, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Expected term (years) | 6.07 | 6.06 | 6.20 |
| Expected volatility | 56% | 60% | 61% |
| Risk-free interest rate | 2.0% | 1.0% | 0.8% |
| Expected dividend rate | 0.0% | 0.0% | 0.0% |

The fair value of PSOs 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, 2022 |
|---|---|
| Expected term (years) | 3.60 |
| Expected volatility | 57% |
| Risk-free interest rate | 1.5% |
| Expected dividend rate | 0.0% |

**13. Defined Contribution Plan**

The Company sponsors a retirement plan in which substantially all of its full-time employees in the U.S. 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 $9.0 million, $5.5 million, and $4.3 million as expense related to the plan for the years ended December 31, 2022, 2021, and 2020, respectively.

## 14. Income Taxes

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Domestic | $ 703,411 | $ 455,314 | $ 189,449 |
| Foreign | (1,686) | (2,333) | (4,090) |
| Total loss before income taxes | $ 701,725 | $ 452,981 | $ 185,359 |

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Current provision for income taxes: | | | |
| Federal | $ — | $ — | $ — |
| State | 6,062 | (14) | 15 |
| International | 1,274 | 1,058 | 1,192 |
| Total current tax provision | 7,336 | 1,044 | 1,207 |
| Deferred tax provision: | | | |
| Federal | — | — | — |
| State | (1,640) | — | — |
| International | — | — | — |
| Total deferred tax provision | (1,640) | — | — |
| Total provision for income taxes | $ 5,696 | $ 1,044 | $ 1,207 |

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.

Beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminated the right to deduct research and development expenditures for tax purposes in the period the expenses were incurred and instead requires all U.S. and foreign research and development expenditures to be amortized over five and fifteen tax years, respectively. Due to this required capitalization of research and development expenditures and the significant taxable income generated as a result of our sale of royalties in July 2022, the Company has recorded current state income tax expense of $6.1 million for the year ended December 31, 2022. The current income tax provision is primarily for state taxes the Company anticipates paying as a result of statutory limitations on the Company's ability to offset expected taxable income with net operating loss carry forwards in certain states.

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Federal statutory income tax rate | 21.0 % | 21.0 % | 21.0 % |
| State income taxes, net of federal benefit | (0.4) | — | — |
| Federal tax credits | 5.9 | 7.2 | 13.7 |
| Other | (0.1) | 0.5 | (0.5) |
| Premium on equity issuance | — | — | 2.2 |
| Nondeductible permanent items | (0.6) | (0.8) | (0.9) |
| Stock-based compensation | (1.2) | 1.3 | 0.9 |
| Uncertain tax positions | (1.2) | (1.4) | (2.7) |
| Change in valuation allowance | (24.0) | (27.9) | (33.9) |
| Foreign rate differential | (0.2) | (0.1) | (0.5) |
| Provision for income taxes | (0.8) % | (0.2) % | (0.7) % |

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, | |
|---|---|---|
| | 2022 | 2021 |
| Deferred tax assets: | | |
| Loss carryforwards | $ 231,835 | $ 306,119 |
| Tax credits | 260,546 | 218,131 |
| Stock options | 39,784 | 33,564 |
| Accruals and reserves | 27,029 | 25,735 |
| Fixed assets and intangibles | 39,233 | 18,263 |
| Liabilities for sales of future royalties | 214,900 | 90,826 |
| Basis difference in equity investments | 8,971 | 3,912 |
| Capitalized research and development costs | 75,335 | — |
| Other | 3,028 | 13,060 |
| Gross deferred tax assets | 900,661 | 709,610 |
| Valuation allowance | (894,518) | (700,669) |
| Total deferred tax assets | 6,143 | 8,941 |
| Deferred tax liabilities: | | |
| In-process research and development | (31,667) | (33,306) |
| Right-of-use lease assets | (6,143) | (8,941) |
| Gross deferred tax liabilities | (37,810) | (42,247) |
| Net deferred tax liabilities | $ (31,667) | $ (33,306) |

As of December 31, 2022 and 2021, the Company had approximately $756.6 million and $1,085.4 million, respectively, of federal net operating loss carryforwards available to reduce future taxable income that will begin to expire in 2031. As of December 31, 2022 and 2021, the Company had approximately $710.0 million and $777.0 million, respectively, of state net operating loss carryforwards available to reduce future taxable income that will begin to expire in 2031.

As of December 31, 2022 and 2021, the Company had federal research tax credit carryforwards of approximately $32.6 million and $22.9 million, respectively, available to reduce future tax liabilities that will begin to expire in 2030. As of December 31, 2022 and 2021, the Company had state research credit carryforwards of $59.9 million and $44.6 million, respectively, available to reduce future tax liabilities that will be carried forward indefinitely.

As of December 31, 2022 and 2021, the Company had federal Orphan Drug Credits of $239.3 million and $208.1 million, respectively, 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.

The valuation allowance increased by $193.8 million and $139.5 million during the years ended December 31, 2022 and 2021, 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, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Balance at beginning of year | $ 55,360 | $ 46,662 | $ 39,954 |
| Additions based on tax positions related to current year | 11,316 | 8,542 | 6,950 |
| Additions for tax positions of prior years | 377 | 356 | 382 |
| Reductions for tax positions of prior years | (259) | (200) | (624) |
| Balance at end of year | $ 66,794 | $ 55,360 | $ 46,662 |

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, 2022, 2021, and 2020, 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 the Company's intention to reinvest the earnings of its non-U.S. subsidiaries in their operations. As of December 31, 2022, the Company had not made a provision for any incremental foreign withholding taxes on approximately $10.9 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, forty state tax jurisdictions, and ten foreign countries. The federal and state income tax returns from inception to December 31, 2022 remain subject to examination.

## 15. Commitments and Contingencies

The Company has various manufacturing, construction, 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.

Manufacturing and service contract obligations primarily relate to the manufacture of inventory for our approved products, the majority of which are due in the next 12 months.

As of December 31, 2022, the aggregate payments under contractually-binding manufacturing and service agreements are as follows (in thousands):

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| | 2023 | 2024 | 2025 | Total |
| Manufacturing and Services | $ 22,892 | $ 4,467 | $ 1,597 | $ 28,956 |

The terms of certain of the Company's licenses, royalties, development and collaboration agreements, as well as other research and development activities, require the Company to pay potential future milestone payments based on product development success. The amount and timing of such obligations are unknown or uncertain. These potential obligations are further described in "Note 8. License and Research Agreements."

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.

## 16. Related Party Transaction

In July 2022, the Company entered into an agreement with a non-profit foundation in which two of the Company's board members, including the Company's Chief Executive Officer, are also board members of the foundation, whereby a $1.0 million contribution will be paid out to the foundation over a four-year period, beginning in the third quarter of 2022, to support rare disease education and awareness. As a result, the Company recorded $0.3 million as research and development expense for this agreement for the year ended December 31, 2022.

## 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, 2022, 2021, and 2020 (in thousands, except share and per share data):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Numerator: | | | |
| Net loss | $ (707,421) | $ (454,025) | $ (186,566) |
| Denominator: | | | |
| Weighted-average shares used to compute net loss per share, basic and diluted | 69,914,225 | 67,795,540 | 60,845,550 |
| Net loss per share, basic and diluted | $ (10.12) | $ (6.70) | $ (3.07) |

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, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Options to purchase common stock, RSUs, and PSUs | 11,290,935 | 8,214,063 | 8,532,236 |
| Employee stock purchase plan | 7,581 | 3,511 | 2,626 |
| Common stock warrants | — | — | 29,449 |
| | 11,298,516 | 8,217,574 | 8,564,311 |

## 18. Accumulated Other Comprehensive Loss

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

| | Year Ended December 31, | |
|---|---|---|
| | 2022 | 2021 |
| Cumulative foreign currency translation adjustment | $ (845) | $ (121) |
| Unrealized loss on securities available-for-sale | (5,728) | (1,283) |
| Total accumulated other comprehensive loss | $ (6,573) | $ (1,404) |

**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) THE TYPE THAT THE REGISTRANT TREATS A PRIVATE OR CONFIDENTIAL.**

# Commercial Master Service Agreement

Between

Ultragenyx Pharmaceutical Inc.
60 Leveroni Court
Novato, CA 94949 USA

(Herein known as “UGX”)

And

BSP Pharmaceuticals S.p.A.
via Appia km 65,561 04013 Latina Scalo (LT), Italy

(Herein known as “BSP”)

Hereinafter referred to individually as a “Party” and together as the “Parties”

This Commercial Master Service Agreement (“AGREEMENT”) is made as of the 22nd day of February, 2021 (“EFFECTIVE DATE”), by and between UGX (on behalf of itself and its Affiliates and subsidiaries), and BSP.

## Preamble

***Whereas***, UGX is a company engaged in the pharmaceutical field focusing on development of rare disease therapies and has obtained regulatory approval to market certain medicinal products based on active pharmaceutical ingredients;

***Whereas***, BSP is a contract development and manufacturing organization focused on innovative products and has the know-how, expertise, capability, experience and the infrastructure necessary to manufacture certain DRUG PRODUCTS subject to and in accordance with the terms hereof;

***Whereas,***UGX wishes to establish a contractual relationship with BSP for the development, manufacturing, supply, RELEASE and store DRUG PRODUCTS for UGX as set forth in the respective sections of this AGREEMENT;

***NOW THEREFORE****,* in consideration of the foregoing, both PARTIES agree to work in a partnership model and are committed to establish the appropriate level of trust and transparency. Each PARTY hereto has a duty of good faith and fair dealing in connection with its performance under this AGREEMENT. Each PARTY shall perform its obligations under this AGREEMENT in a diligent, legal, ethical and professional manner so as to advance the purposes and intend of this AGREEMENT.

Hereby agree as follows:

## 1. Contents

# 1. Definition

**a.** **ADDITIONAL SERVICES**means any service provided by BSP and approved by both PARTIES, other than the MANUFACTURING SERVICES.

**b.** **AFFILIATE**shall mean with respect to a Party, any person, corporation, company, partnership or other entity that controls, is controlled by, or is under common control with that Party. For the purpose of this definition, “control” shall mean direct ownership of fifty (50%) or more of the shares of stock entitled to vote for the election of directors, in the case of a corporation, or fifty percent (50%) of more of the equity interest in the case of any other type of legal entity, status as a general partner in any partnership, or any other arrangement whereby the entity or person controls or has the right to control the board of directors or equivalent governing body of a corporation or other entity, or the ability to cause the direction of the management or policies of a corporation or other entity.

**c.** **API/DRUG SUBSTANCE** means the active pharmaceutical ingredient or drug substance identified on the applicable PRODUCT SCHEDULE, or any intermediate or component of such active pharmaceutical ingredient or drug substance.

**d.** **API QUANTITY DISPENSED** shall mean with respect to a DRUG PRODUCT for any relevant period, the difference between (a) the sum of (i) the total quantity of the API for such DRUG PRODUCT that [***], plus (ii) the the total quantity of such API that [***]; less (b) the sum of (i) the total quantity of such API that [***], plus (ii) the quantity of such API [***]. For clarity, the API QUANTITY DISPENSED shall include API [***] or [***] while in [***] or [***].

**e.** **APPLICABLE LAWS** shall mean all applicable ordinances, rules, regulations, directives, laws, guidelines, guidance, statutes, requirements, national and supranational, as amended from time to time, and court orders of any Authority to the extent applicable to the parties, including, without limitation, (a) cGMP, and (b) those of any REGULATORY AUTHORITY located where the MANUFACTURING SERVICES or ADDITIONAL SERVICES will be performed. APPLICABLE LAWS include, without limitation, the United States Food, Drug, and Cosmetic Act, as amended (21 U.S.C. § 301 et seq., 21 CFR Parts 210, 211 and 11), and the rules and regulations promulgated thereunder, and Directive 2001/83/ EC and amendments, EudraLex, Volume 4, Good Manufacturing Practice (GMP) guidelines, Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use 2013/C 343/01), (EU) No 440 536/2014, ICH Guidelines and other national requirements as per territories mentioned.

**f.** **BANKRUPTCY** has the meaning set forth in Section 20.2.7.

**g.** **BACKGROUND INTELLECTUAL PROPERTY** has the meaning set forth in Section 13.1.

**h.** **BATCH(ES)**shall mean a specific quantity of material produced in a process or series of processes so that it is expected to be homogeneous within specified limits. In the case of continuous production, a BATCH may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval.

i. **BATCH DOCUMENTATION** shall mean the complete set of information, data and results applicable to one batch relating to the MANUFACTURING, control and RELEASE of the particular BATCH, including but not limited to the applicable executed BATCH records, laboratory control results and in-process control results, any applicable deviation and investigation reports and the CERTIFICATE OF ANALYSIS, certificate of confirmation, change requests, which are required to comply with all applicable cGMP requirements.

j. **BINDING FORECAST** has the meaning set forth in Section 8.3.1.

k. **BSP INVENTION** has the meaning set forth in Section 13.4.

l. **BUSINESS DAY** shall mean each day of the week on which a Party`s offices are open for business (usually any day except Saturday, Sunday and legal holidays in Italy, Switzerland and United States of America).

m. **CALENDAR QUARTER** shall mean the respective periods of three (3) consecutive calendar months ending March 31st, June 30th, September 30th and December 31st.

n. **CALENDAR MONTH** shall mean means any of the twelve (12) calendar months of a CALENDAR YEAR.

o. **CALENDAR YEAR** means a period of twelve consecutive months from January 1st to December 31st.

p. **CERTIFICATE OF ANALYSIS or CoA** shall mean a document detailing test procedures, SPECIFICATION and results and signed by BSP qualified person to assure results are accurate and complete and certifying that a particular BATCH was MANUFACTURED and tested according to the MANUFACTURING process then in effect and is compliant with all APPLICABLE LAWS and cGMP requirements. The CoA includes the Batch Certificate information and statement.

q. **CLAIM** has the meaning set forth in Section 14.1.

r. **CONFIDENTIAL INFORMATION** has the meaning set in forth in Section 18.1.

s. **DECOMMISSIONING** means the activities set forth in Article 21, including the process of verifying that all UGX and BSP contractual commitments have been met and that all data, information, documents, software, DRUG PRODUCT, PURCHASED MATERIAL, samples, FOC MATERIAL and UGX property have either been returned to UGX and/or destroyed by BSP, at UGX discretion and expenses.

t. **DEDICATED EQUIPMENT** shall mean all Equipment that is used only for the Drug Product and that the Parties determine in good faith as necessary to perform any part of the MANUFACTURING SERVICES and ADDITIONAL SERVICES.s

u. **DELIVERY DATE** means, with respect to a quantity of DRUG PRODUCT ordered by UGX in a PURCHASE ORDER, the date indicated in the PURCHASE ORDER on which UGX requires the quantity of DRUG PRODUCT to be available for delivery after its RELEASE.

v. **DRUG PRODUCT** means the form of medicinal product to be MANUFACTURED by BSP as further described in the applicable PRODUCT SCHEDULE.

w. **EQUIPMENT** means any equipment system or machinery, including the DEDICATED EQUIPMENT, owned, provided to, and used by BSP for the MANUFACTURING, holding, processing, testing, RELEASE and/or packaging of UGX`s DRUG PRODUCT.

x. **EXECUTIVE LEADERSHIP** shall mean for the purpose of this AGREEMENT any representatives ([***] or [***]) to each Party having a [***].

y. **FACILITY** shall mean the BSP manufacturing site located in via Appia km 65,561 - 04013 Latina Scalo (LT), Italy.

z. **FOC (Free of Charge) MATERIAL** means API/DRUG SUBSTANCE and other materials supplied by UGX to BSP free of charge.

aa. **FORCE MAJEURE EVENT** shall have the meaning as provided in Section 19.

bb. **cGMP** shall mean Current Good Manufacturing Practices as regulated under APPLICABLE LAW. Current Good Manufacturing Practice (cGMP) is the applicable term in the United States. For the purpose of this AGREEMENT, the terms “GMP” and “cGMP” are equivalent.

cc. **LATENT DEFECT** means a defect or a non-conformity of FOC MATERIAL or DRUG PRODUCT, as the case may be, which was already present at the time of delivery but was not and could not be detectable upon (i) reasonable physical inspection and (ii) testing using the methodology specified in the QTA, this latter only in the event that testing on DRUG PRODUCT is performed by UGX or a third independent laboratory pursuant to Section 10.6.

dd. **IMPROVEMENT** means technical and business process optimization that is beneficial for the MANUFACTURING, UGX’s DRUG PRODUCT quality, financial aspect or supply of UGX`s DRUG PRODUCT.

ee. **INDEMNIFICATION NOTE** has the meaning set forth in Section 14.2.

ff. **INDEMNIFIED PARTY** has the meaning set forth in Section 14.2.

gg. **INDEMNIFYING PARTY** has the meaning set forth in Section 14.2.

hh. **[***] FORECAST**has the meaning set forth in Section 8.1.

ii. **INTELLECTUAL PROPERTY RIGHTS** or **IP RIGHTS** means rights in patents, patent applications (including all utility and design patents and patent applications), know how, INVENTIONS (whether or not patented or patentable), trade secrets, copyrights, trademarks, service marks, trade names, internet domain names, rights in designs, rights in get-up and trade dress, goodwill and the right to sue for passing off or unfair competition, copyrights, (including all computer applications, programs and other software, including without limitation operating software, network software, firmware, middleware, and design software rights in computer software and databases), database rights, industrial property rights, moral rights of authors, rights to use and protect the confidentiality of, confidential information, utility models, all rights of renewal, continuations, divisions, extensions and the like relating to the foregoing, and other intellectual property rights, in each case whether registered or unregistered and including any applications and rights to apply for the grant of any such rights and all rights and forms of protection having an equivalent or similar effect anywhere in the world– and the like that are afforded (or may be afforded upon action by a REGULATORY AUTHORITY, such as the United States patent Office) Intellectual Property Rights.

jj. **INVENTIONS**shall mean all formulas, processes, techniques, compounds, compositions, data, copyrightable material, know-how, improvements and inventions, whether or not patentable or copyrightable, which are made, conceived, learned or reduced to practice, either alone or jointly by a Party during the performance of the MANUFACTURING SERVICES and ADDITIONAL SERVICES under this AGREEMENT.

kk. **JOINT STEERING COMMITTEE** shall mean the committee selected by the Parties in accordance with the criteria set out under Section 5 of this AGREEMENT.

**ll.** **JOINT WORKING TEAM** shall mean the team selected by the STEERING COMMITTEE in accordance with the criteria set out under Section 5 of this AGREEMENT.

**mm.** **JOINT WORKING TEAM LEAD** has the meanings set forth in Section 5.12.

**nn.** **LOSSES** has the meaning set forth in Section 14.1.

**oo.** **[***]** shall mean the [***]that [***] on an [***] as agreed in writing by the Parties and set forth in the PRODUCT SCHEDULE.

**pp.** **MANUFACTURE** or **MANUFACTURING** or **MANUFACTURED**means any steps, processes and activities that relate to the manufacturing of DRUG PRODUCT, including without limitation, the quality control and release of FOC MATERIALS, the RELEASE, the process and the filling and packaging for transport of DRUG PRODUCT, as performed by BSP in accordance with the SPECIFICATION, cGMP, this AGREEMENT and QTA conditions.

**qq.** **MANUFACTURING DATE** shall be the date confirmed in writing by BSP subject to UGX's approval for the MANUFACTURE of a certain BATCH of DRUG PRODUCT.

**rr.** **MANUFACTURING SERVICES** means all activities related to MANUFACTURING of DRUG PRODUCT as described in this AGREEMENT, including all activities and material involved in converting FOC MATERIAL into DRUG PRODUCT according to the quality standards set forth in the QTA.

**ss.** **MANUFACTURING SERVICE FEE** means the price related cost of all activities involved in converting FOC Materials into DRUG PRODUCT (including, without limitation and except as otherwise provided in this AGREEMENT, costs of in-process control, quality assurance, quality control and RELEASE, bulk packaging, storage of FOC MATERIALS, disposal of waste produced from the MANUFACTURE of DRUG PRODUCT or performance of the SERVICES). MANUFACTURING SERVICE FEE shall be set forth on each applicable PRODUCT SCHEDULE.

**tt.** **MATERIAL CHANGE IN CONTROL** shall mean any of the following: (i) the sale or disposition of all or substantially all of the assets of a Party to another entity, (ii) the acquisition by another entity, of more than 50% of a Party's outstanding shares of voting capital stock (e.g. capital stock entitled to vote generally for the election of directors), or (iii) the merger or consolidation of a Party with or into another corporation.

**uu.** **NON-CONFORMING** means a BATCH that fails to conform to the quality and regulatory requirements of this AGREEMENT and the QTA, including the DRUG PRODUCT SPECIFICATIONS.

**vv.** **OFFER** shall mean BSP's quotation containing the prices and details of the MANUFACTURING SERVICES and/or ADDITIONAL SERVICES subject to UGX's request.

**WW.** **PERSON IN PLANT** shall mean UGX's representative(s) present at Facility.

**xx.** **PERMISSIBLE FLUCTUATION** has the meaning set forth in Section 8.4.1.

**yy.** **PRODUCT SCHEDULE** means a product specific-agreement meeting the requirements for a PRODUCT SCHEDULE set forth in this Agreement, substantially in the form attached hereto as Appendix I, executed by both UGX and BSP, that engages BSP to provide UGX with specified MANUFACTURING SERVICES and ADDITIONAL SERVICES.

**zz.** **PURCHASE ORDER** shall mean either a written or electronic PURCHASE ORDER for MANUFACTURING SERVICES and/or ADDITIONAL SERVICES placed and issued by UGX with a corresponding PURCHASE ORDER number to BSP in accordance with this AGREEMENT.

**aaa.** **PURCHASED MATERIAL** shall mean all materials, apart from FOC MATERIALS, that include raw materials, excipients, packaging and labeling materials, components, disposable equipment and change parts, purchased by BSP used by this latter in the MANUFACTURING of DRUG PRODUCT and in the provision of MANUFACTURING SERVICES.

**bbb.** **QUALITY AND TECHNICAL AGREEMENT or QTA**shall mean the Technical and Quality Agreement accepted by the Parties and attached to this AGREEMENT under its Appendix III.

**ccc.** **QUARANTINE SHIPMENT** shall mean a shipment of FOC MATERIAL by UGX or of DRUG PRODUCT by BSP before the issuance of relevant certificates of analysis in accordance with the QTA.

**ddd.** **RECORDS** shall have the meaning set forth in Section 12.1.

**eee.** **REGULATORY AUTHORITY** shall mean any supranational, national, regional, state or local government, court, governmental agency, authority, board, bureau, instrumentality or regulatory body, including FDA and EMA.

**fff.** **REIMBURSABLE VALUE** means the value set forth in the applicable PRODUCT SCHEDULE determined by mutual agreement of the Parties for loss of FOC MATERIAL for the reasons set forth in Section 10.8.

**ggg.** **RELEASE**shall mean DRUG PRODUCT that is quality-released by BSP's qualified person as per QTA.

**hhh.** **RENEWAL TERM** shall have the meaning set forth in Section 20.1.

**iii.** **RETENTION PERIOD** shall have the meaning set forth in Section 12.2.

**jjj.** **SPECIFICATIONS** shall mean a list of tests, references to analytical procedures, and appropriate acceptance criteria that are numerical limits, ranges, or other criteria for the test described. It establishes the set of criteria to which a material or DRUG PRODUCT should conform to be considered acceptable for its intended use. Conformance to specification means that the material or DRUG PRODUCT, when tested according to the listed analytical procedures, meets the listed acceptance criteria. For the sake of clarity, DRUG PRODUCT SPECIFICATIONS are provided by UGX.

**kkk.** **STORAGE FEE** shall mean the fee paid by UGX for storing the DRUG PRODUCT at FACILITY in accordance with this AGREEMENT and the relevant PRODUCT SCHEDULE

**lll.** **TARGET YIELD** shall have the meaning set forth in Section 10.11.

mmm. **TERM** shall have the meaning set forth in Section 20.1.

**nnn.** **THIRD-PARTY** shall mean any person other than UGX, BSP and their respective AFFILIATES.

**ooo.** **TERRITORY** shall mean the following countries: EU, USA, Japan, or any different country as agreed by the Parties in the QTA during the term of this AGREEMENT after the EFFECTIVE DATE.

**ppp.** **TRANSFER REQUEST** has the meaning set forth in Section 20.4.

**qqq.** **UGX INVENTION** has the meaning set forth in Section 13.3.

rrr. **WORK IN PROCESS** means filled and stoppered vials of DRUG PRODUCT at any time prior to the RELEASE.

## 2. Scope of the Agreement

a. UGX hereby retains BSP to perform the MANUFACTURING SERVICES and the ADDITIONAL SERVICES for the benefit of UGX in accordance with the terms of this AGREEMENT and the applicable PRODUCT SCHEDULE, the applicable DRUG PRODUCT SPECIFICATIONS, the applicable PURCHASE ORDER(S) and the QTA. On the terms set forth herein, UGX will pay the MANUFACTURING SERVICES FEE and ADDITIONAL SERVICES fee, if any, as agreed between the Parties pursuant to this AGREEMENT.

b. It is understood that:

1. UGX is not obliged to retain BSP as exclusive manufacturer for DRUG PRODUCT;
2. BSP will perform the MANUFACTURING SERVICES and the ADDITONAL SERVICES on a non-exclusive basis.

c. A description of the MANUFACTURING SERVICES and ADDITIONAL SERVICES shall be contained in any relevant PRODUCT SCHEDULE, consistent with the form attached hereto as Appendix I.

d. From time to time during the term of this AGREEMENT, BSP and UGX may enter into PRODUCT SCHEDULES, which shall be executed by duly authorized signatories of each Party. Each PRODUCT SCHEDULE shall be subject to and deemed to be part of and regulated by this AGREEMENT. No PRODUCT SCHEDULE, or any modification thereto, shall be attached to or made a part of this AGREEMENT without first being executed by the Parties hereto in writing, specifically referencing this AGREEMENT.

e. This AGREEMENT will form the basis for the issuance of PURCHASE ORDERS by UGX to BSP. This AGREEMENT (including the applicable PRODUCT SCHEDULE and QTA) regulates and forms an integral part of such PURCHASE ORDERS. In addition, each PURCHASE ORDER will be subject to and deemed to be a part of this AGREEMENT. The Parties acknowledge that any document shared among them under this AGREEMENT, including any PURCHASE ORDER and other business form or written authorization used by UGX or BSP, may include or refer to a Party's general terms and conditions. The Parties agree that any of such general terms and conditions of the Parties shall not (i) apply to any transactions under this AGREEMENT and (ii) have any effect on the rights, duties or obligations of the Parties as detailed in this AGREEMENT, any PURCHASE ORDER, PRODUCT SCHEDULE and the QTA or otherwise modify this AGREEMENT, any PURCHASE ORDER, PRODUCT SCHEDULE and the QTA, regardless of any failure of UGX or BSP to object to such Party's general terms and conditions.

f. Each PRODUCT SCHEDULE takes effect upon execution by the Parties and shall continue to be in force until this AGREEMENT is terminated for whatever reason pursuant to Section 20 of this AGREEMENT. Each PRODUCT SCHEDULE may be terminated independently of the rest of this AGREEMENT, with any provision of this AGREEMENT relevant to termination applying only to that specific PRODUCT SCHEDULE. As soon as practicable and in connection with the execution of any PRODUCT SCHEDULE, as applicable, the Parties shall enter into appropriate QTA. The obligations set forth in the QTA, and any amendments thereto, shall become part of, and be incorporated into, this AGREEMENT and the relevant PRODUCT SCHEDULE and regulate the execution of any of MANUFACTURING SERVICES and ADDITONAL SERVICES detailed herein.

g. In case of any conflict between the QTA and this AGREEMENT (to which the PURCHASE ORDER(S) and the applicable PRODUCT SCHEDULE that includes the OFFER approved by UGX, are an integral part) this AGREEMENT shall prevail, unless otherwise expressly agreed either in the QTA, PURCHASE ORDER(S) or applicable PRODUCT SCHEDULE that (i) makes reference to the specific section of this AGREEMENT to be overruled by the QTA, and (ii) has been approved in writing by both Parties; provided, however, that to the extent such conflict relates to the quality provisions of the QTA, the QTA will take precedence.

h. Attached to this AGREEMENT are the following Appendixes which form an integral part of this AGREEMENT:

| | |
|---|---|
| Appendix I | Product Schedule |
| Appendix II | Compliance |
| Appendix III | QUALITY AND TECHNICAL AGREEMENT (QTA) |

## 3. BSP Responsibilities

a. BSP shall comply with this AGREEMENT, all its Appendixes, cGMP and with recognized industry standards in the performance of the MANUFACTURING SERVICES and ADDITIONAL SERVICES.

b. BSP shall (i) make available and maintain the manufacturing site, the EQUIPMENT, as required by cGMP, BSP's SOPs and the QTA, and (ii) employ and dedicate to the performance of MANUFACTURING SERVICES and ADDITIONAL SERVICES a sufficient number of trained and competent personnel with relevant knowledge and experience, and (iii) ensure capacity to store the FOC MATERIAL and the excipients needed for the MANUFACTURING SERVICES and the ADDITIONAL SERVICES within the timeframe set forth in this AGREEMENT and in accordance with the QTA.

c. BSP will notify UGX immediately of any potential failure to deliver the DRUG PRODUCT within the agreed timelines.

d. BSP will render the MANUFACTURING SERVICES and the ADDITIONAL SERVICES in a professional and workmanlike manner in accordance with applicable industry standards and this AGREEMENT, including the QTA.

e. BSP will comply with any exposure guidelines set forth in any material safety data sheets provided by UGX for the DRUG PRODUCT. BSP will promptly inform UGX of any adverse environmental, health or safety events related to the MANUFACTURING of the DRUG PRODUCT.

## 4. UGX Responsibilities

a. UGX shall be responsible to:

1. provide BSP with FOC MATERIAL's material safety data sheet to MANUFACTURE the DRUG PRODUCT.

2. provide BSP with FOC MATERIAL necessary to perform the MANUFACTURING SERVICES in line with Section 6 of this AGREEMENT and according to all provisions in the relevant PRODUCT SCHEDULE, where applicable. FOC MATERIAL shall be (i) suitable for the MANUFACTURING of the DRUG PRODUCT, (ii) compliant with APPLICABLE LAWS, and (iii) provided with the relevant documentation, including the certificate of analysis.

3. pay BSP for the MANUFACTURING SERVICES and ADDITIONAL SERVICES in accordance with the pricing, milestones and payment terms set forth in the applicable PRODUCT SCHEDULE, PURCHASE ORDER(s) and the terms of this AGREEMENT.

4. perform any other obligations expressly assigned to UGX in this AGREEMENT, the relevant PRODUCT SCHEDULE, any PURCHASE ORDER and the QTA.

b. UGX shall comply with this AGREEMENT, all its Appendixes and the QTA.

## 5. Governance Model

a. The governance model set forth herein below encompasses a JOINT STEERING COMMITTEE and a JOINT WORKING TEAM focusing on operational execution. The JOINT WORKING TEAM will be led by the JOINT WORKING TEAM LEADS (as defined below).

b. Within [***] CALENDAR DAYS of the EFFECTIVE DATE or at UGX's request, the Parties shall establish a JOINT STEERING COMMITTEE consisting of at least [[***] ([***]) [[***]] members to provide overall strategic vision and

direction for the Parties to perform their respective obligations under this AGREEMENT, any of its Appendixes and the QTA. Each Party will nominate minimum [***]([***])] JOINT STEERING COMMITTEE members with [***] from each of UGX and BSP having oversight for quality activities, and with [***]from each of UGX and BSP having oversight for manufacturing and supply chain activities.

c. Either Party may replace its JOINT STEERING COMMITTEE members by written notice to the other Party.

d. The JOINT STEERING COMMITTEE members shall be appropriately qualified and experienced in order to make a meaningful contribution to the JOINT STEERING COMMITTEE meetings.

e. The responsibilities of the JOINT STEERING COMMITTEE are to:

1. establish and maintain an effective and efficient collaboration between the Parties;
2. confirm the JOINT WORKING TEAM leads by each Party;
3. resolve any dispute or disagreement among the Parties regarding the execution of this AGREEMENT or the progress of the MANUFACTURING SERVICES or ADDITIONAL SERVICES that cannot be resolved at the JOINT WORKING TEAM level;
4. act as escalation body for issue resolution;
5. define the framework for continuous IMPROVEMENT, mutual long-term objectives and priorities;
6. reviewing and validating any amendment or update to this AGREEMENT (including any updated PURCHASE ORDER and modifications to the QTA);
7. any other topics assigned to it in compliance with this AGREEMENT or following a mutual decision of the Parties.

f. The JOINT STEERING COMMITTEE, which shall conduct its discussions in good faith with a view to operating to the mutual benefit of the Parties, shall meet as often as its members may determine and in any case at a minimum [***] per CALENDAR YEAR. Meetings can be held face-to-face or by teleconference. Either Party may request a meeting within [[***] ([***])BUSINESS DAYS in in case it is perceived as necessary.

g. The agenda (including any pre-read material, if any) shall (i) include all relevant topics to be discussed between the JOINT STEERING COMMITTEE members and (ii) be distributed in an agreed timeframe prior to the related meeting between such JOINT STEERING COMMITTEE members.

h. Each Party may invite other representatives with particular skills, who are part of their respective organizations to attend such JOINT STEERING COMMITTEE meetings, where it is considered to be relevant and appropriate.

i. All decisions of the JOINT STEERING COMMITTEE shall be made in good faith, in the best interests of the compliant performance of this AGREEMENT, and be [***] by all of its members or their designated representatives. All such decisions will be reflected in written meeting reports which summarily address topics discussed, delegation of work, schedules and decisions of the JOINT STEERING COMMITTEE. In the event that the JOINT STEERING COMMITTEE is unable to reach a decision on any matter critical to business or DRUG PRODUCT after good faith attempts to resolve such disagreement in a commercially reasonable fashion within [***] BUSINESS DAYS, then such matter should be referred to the [***]of both Parties who should use reasonable and good faith efforts to reach a decision by consensus within [***] BUSINESS DAYS after such matter is referred to them or such other time period as is agreed to by the Parties.

j. If the [***] does not reach an agreement in accordance with Section 5.9, either Party may commence dispute resolution proceedings in accordance with the relevant provisions set out in Section 23.8.

k. The JOINT STEERING COMMITTEE members shall draft agenda and take minutes of its meetings and resolutions, which shall be promptly circulated to the Parties after each meeting for adjustment and agreement, unless otherwise mutually agreed by the Parties. In case of any disagreement Sections 5.9 and 5.10 shall apply.

l. Within [***] CALENDAR DAYS of the EFFECTIVE DATE or at UGX's request, the Parties shall establish a JOINT WORKING TEAM appointing [***] subject matter expert each with primary responsibility for day-to-day interactions with the other Party to allow the compliant and timely performance of the MANUFACTURING SERVICES and ADDITIONAL SERVICES under this AGREEMENT (each, a "JOINT WORKING TEAM LEAD"). Thus, the minimum size of the JOINT WORKING TEAM shall be of [***] JOINT WORKING TEAM LEADS.

m. The JOINT WORKING TEAM LEADS may invite additional members. Such members shall be appropriately qualified and experienced in order to make a meaningful contribution to the JOINT WORKING TEAM meetings.

n. Either Party may replace its JOINT WORKING TEAM LEADS and members, where applicable, by written notice to the other Party. Should UGX not be satisfied of BSP's JOINT WORKING TEAM LEAD, UGX may communicate such dissatisfaction to BSP, which will (i) check and clarify with UGX the reasons for such dissatisfaction and (ii) promptly substitute the relevant JOINT WORKING TEAM LEAD. While exploring alternatives for a new JOINT WORKING TEAM LEAD that could be satisfactory for UGX, BSP shall guarantee full project management support.

o. The responsibilities of the JOINT WORKING TEAM are to:

1. drive and improve performance of MANUFACTURING SERVICES and ADDITIONAL SERVICES, if any, including the TARGET YIELD, and the JOINT WORKING TEAM functionality;
2. establish, manage and review routinely other relevant key performance indicators applicable to the MANUFACTURING SERVICES and ADDITIONAL SERVICES whether agreed and discussed in writing by the Parties in advance;
3. manage MANUFACTURING SERVICES and ADDITIONAL SERVICES risks, including lead times and safety stock management of PURCHASED MATERIALS;
4. overseeing and monitoring the MANUFACTURING and manage any and all issues related to the MANUFACTURING SERVICES and the ADDITIONAL SERVICES;
5. maintain a collaborative and constructive relationship (at operational level);
6. facilitate expeditious resolution of any issues, also in accordance with the instructions from the JOINT STEERING COMMITTEE, if received;
7. propose any IMPROVEMENT to the JOINT STEERING COMMITTEE functionality.

p. The JOINT WORKING TEAM shall meet as often as the JOINT WORKING TEAM MEMBERS may determine, but in any event not less than [***]per [***]. Meetings can be held face-to-face or by teleconference.

q. The JOINT WORKING TEAM shall conduct its discussion in good faith with a view to operating to the mutual benefit of the Parties.

r. All decisions of the JOINT WORKING TEAM shall be made in good faith in the best interest of the timely and compliant performance of this AGREEMENT, including the QTA. In the event that the JOINT WORKING TEAM is unable to reach a decision on any matter after good faith attempts to resolve such disagreement in a commercially reasonable fashion within [***] BUSINESS DAYS, then such matter should be referred to and decided by the JOINT STEERING COMMITTEE which shall decide according to Sections 5.09., 5.10. and 5.11.

s. BSP's JOINT WORKING TEAM LEAD shall take minutes of meeting and resolution, which shall be circulated in an agreed time frame after each meeting for adjustment and agreement.

## 6. FOC MATERIALS

1. UGX shall, [***] supply BSP with a sufficient quantity of FOC MATERIALS for BSP to perform the MANUFACTURING SERVICES and/or ADDITIONAL SERVICES according to any applicable PURCHASE ORDER and this AGREEMENT. BSP will store FOC MATERIALS in accordance with the FOC MATERIALS SPECIFICATIONS and the QTA. BSP shall not use any FOC

MATERIALS for any purpose other than the performance of the MANUFACTURING SERVICES and/or ADDITIONAL SERVICES. UGX will promptly inform BSP if it encounters supply problems with FOC MATERIALS supplier, including delays and/or delivery of FOC MATERIALS under this AGREEMENT. UGX must take reasonable measures to mitigate and resolve such problems.

2. UGX will maintain the title on all FOC MATERIAL, any WORK IN PROCESS and DRUG PRODUCT at each and every stage of the MANUFACTURING, including the storage. BSP will custody FOC MATERIAL, any WORK IN PROCESS and DRUG PRODUCT free and clear of all liens and encumbrances.

3. UGX shall deliver, or cause to be delivered, sufficient quantities of FOC MATERIAL (i) not earlier than [***] and no later than [***] before the agreed [***], unless otherwise provided in the applicable PRODUCT SCHEDULE, and (ii) accompanied by such certificates of analysis and other documents as required by the applicable QTA. Should FOC MATERIAL not be released according to the QTA, UGX shall be entitled to deliver, at [***] costs, such FOC MATERIAL to BSP as QUARANTINED SHIPMENT, provided that all such FOC MATERIALS in QUARANTINED SHIPMENT shall not be used for the MANUFACTURE of DRUG PRODUCT until the relevant certificate of analysis is issued by the relevant manufacturer. Should FOC MATERIAL not be available to be delivered at BSP at least [***] before the [***], then UGX shall immediately notify BSP thereof. Promptly thereafter, the Parties shall discuss in good faith if BSP can (i) meet the original DELIVERY DATE using its [***] to do so, or (ii) adjust the new MANUFACTURING DATE based on BSP's production plan to the extent consistent with BSP's obligations vis-a-vis its other customers and the estimated delivery date of FOC MATERIAL; provided that in all cases BSP shall use [***] to schedule the new MANUFACTURING DATE as soon as possible unless otherwise advised by UGX. Should the adjustment of the new MANUFACTURING DATE not be acceptable to UGX, the relevant production shall be cancelled and UGX shall remain obligated to [***] pursuant to the provision of Section [***].

4. Any FOC MATERIALS will be accompanied by a certificate of analysis and any related relevant documentation. BSP shall not incorporate any of such FOC MATERIALS into the DRUG PRODUCT in the case the certificate of analysis is not available. At the incoming of FOC MATERIAL, BSP shall run a visual inspection to check the physical integrity of the packaging and a verification of the documentation received in connection with such FOC MATERIAL. If BSP's incoming inspection of packaging and documentation reveals any damages or documentary inconsistencies, BSP shall immediately notify in writing to UGX the outcome of such inspection.

5. In addition, BSP shall conduct incoming tests on FOC MATERIALS in accordance with the related PRODUCT SCHEDULE and the QTA. If the testing reveals that such FOC MATERIALS do not comply with the applicable FOC MATERIALS SPECIFICATIONS, BSP shall give immediately UGX a written notice of such non-compliance in accordance with the terms set forth in this AGREEMENT and in the QTA. Upon receipt of the notice of non-compliance and within the timing agreed between the Parties, but in any case in time for the MANUFACTURING DATE, UGX may request BSP to perform, at [***] costs (previously approved in writing by UGX), those additional tests and controls on the FOC MATERIAL to determine FOC MATERIAL's compliance or non-compliance with the applicable FOC MATERIALS SPECIFICATIONS, in accordance with cGMP, provided that BSP has the capabilities and capacities to conduct such tests and controls. BSP shall promptly inform UGX if the required capabilities or capacities are not available for a requested test or control. UGX shall lead the investigation of any purported non-compliance of any FOC MATERIAL. BSP shall cooperate with UGX's reasonable requests for assistance in connection with its evaluation hereunder.

6. Unless otherwise agreed by the Parties, UGX shall replace such FOC MATERIALS non-conforming with the relevant specifications and/or defected pursuant to 6.4 and 6.5 with an equivalent quantity of FOC MATERIALS meeting the applicable FOC MATERIALS specifications, at [***], in time for the MANUFACTURING DATE. UGX shall promptly provide instructions to BSP for the disposal or return of FOC MATERIALS non-conforming with the relevant specifications and/or defected. Should BSP not receive any written instruction within [***] CALENDAR DAYS of the notice set forth in Section 6.5 or alternative term agreed upon by the Parties, BSP shall return such FOC MATERIALS non-conforming with the relevant specifications and/or defected to UGX at [***] costs and expenses at the address set forth in the PRODUCT SCHEDULE. Should UGX not be able to replace FOC MATERIALS non-conforming with the relevant specifications and/or defected in time for the originally agreed MANUFACTURING DATE, the Parties shall discuss in good faith if BSP can (i) meet the original DELIVERY DATE using its best efforts to do so, or (ii) adjust the new MANUFACTURING DATE based on BSP's production plan to the extent consistent with BSP's obligations *vis-a-vis* its other customers and the estimated delivery date of FOC MATERIAL; provided that in all cases BSP shall use [***] to schedule the new MANUFACTURING DATE as soon as possible, unless otherwise advised by UGX. Should the adjustment of the new MANUFACTURING DATE not be

acceptable to UGX, the relevant production shall be cancelled and UGX shall remain obligated to pay such part of unused capacity pursuant to the provision of Section 8.8.

7. Except where stated otherwise in a PRODUCT SCHEDULE, BSP will give UGX: (i) a [***]inventory report of [***]-end inventory balance of each lot of the FOC MATERIALS and DRUG PRODUCT for such [***] (including the API QUANTITY DISPENSED for such [***] and the number of BATCHES attempted for such [***]); and (ii) upon UGX's request, [***] physical product inventory per calendar year, which will be conducted by UGX or a designee of UGX, at the date mutually agreed upon by the Parties, *provided that* should such designee of UGX be a consultant then such physical product inventory shall be subject to the execution of a confidentiality agreement between UGX, BSP and such consultant.

8. Not later than [***] CALENDAR DAYS after the end of each [***], BSP shall provide UGX with an accounting, certified by BSP, of the disposition of each lot of the FOC MATERIAL for DRUG PRODUCT for such [***] utilizing BSP's standard format, including the API QUANTITY DISPENSED for such [***]and the number of BATCHES attempted for such [***].

9. Any shipment from UGX or its designee to BSP will be made [***] [***].

## 7. PURCHASED MATERIALS. DEDICATED EQUIPMENT.

a. Except as otherwise provided in each PRODUCT SCHEDULE, it will be BSP's obligation hereunder to purchase, procure, store and test at [***]expense and cost, all PURCHASED MATERIALS needed for the MANUFACTURING in accordance with this AGREEMENT, all its Appendixes and the QTA.BSP shall apply a handling/service fee of [***] for BSP's procuring and maintaining such PURCHASED MATERIALS.

b. PURCHASED MATERIALS will be procured and tested by BSP from sources as agreed on by the Parties in good faith and as set forth in the PRODUCT SCHEDULE and/or QTA. Such PURCHASED MATERIALS shall meet all PURCHASED MATERIALS SPECIFICATIONS and quality requirements set forth in writing by UGX (e.g. in the PRODUCT SCHEDULE and/or QTA). BSP will promptly inform UGX if it encounters supply problems, including delays and / or delivery of non-conforming PURCHASED MATERIALS which could affect the MANUFACTURING of DRUG PRODUCT, as set forth in the QTA.

c. BSP should ensure and maintain, at [***]cost and expense, a dedicated safety stock available of any long lead-time and critical PURCHASED MATERIALS as determined by the Parties in good faith to cover unexpected volumes and/or additional quantities of DRUG PRODUCT in excess of the flexibilities granted under this AGREEMENT and the relevant PRODUCT SCHEDULE. The definition of such safety stock levels should be reviewed periodically and mutually agreed by the JOINT WORKING TEAM as it seems necessary. Inventory for such safety stocks shall be invoiced separately in advance on the basis of a shared plan that shall be initially included in the PRODUCT SCHEDULE and then discussed at the end of any CALENDAR YEAR.

d. PURCHASED MATERIALS shall be invoiced separately and paid by UGX pursuant to Section 11 together with the MANUFACTURING SERVICE FEE or ADDITIONAL SERVICE fee on the basis of the volumes set forth in the BINDING FORECAST.

e. UGX may decide to supply PURCHASED MATERIALS to BSP. In such a case, such PURCHASE MATERIALS shall be included in the list of FOC MATERIALS outlined in the PRODUCT SCHEDULE.

f. BSP will not change PURCHASED MATERIALS suppliers or others suppliers of PURCHASED MATERIALS without the prior written consent of UGX. BSP will give UGX prior written notice of any such proposed change in accordance with the terms of the QTA.

g. If requested, BSP shall maintain [***]backup (or such other mutually agreed upon quantity and costs set forth in the applicable PRODUCT SCHEDULE) of each of the change parts specified in the applicable PRODUCT SCHEDULE. UGX shall [***] the [***] set forth in the PRODUCT SCHEDULE, plus [***] of [***].

h. Dedicated Equipment. Unless otherwise agreed upon in writing by the Parties in the PRODUCT SCHEDULE, BSP shall be the owner of the DEDICATED EQUIPMENT and agree to maintain and manage in full functionality under its own responsibility. For the sake of clarity, when applied to freezers for which UGX has corresponded a contribution, as set forth in the relevant PRODUCT SCHEDULE, the definition of DEDICATED EQUIPMENT shall be extended to cover such equipment and BSP shall use the freezers exclusively for UGX when DRUG PRODUCTS are stored in there.

i. BSP will operate and use the DEDICATED EQUIPMENT in accordance with the instructions set forth in the DEDICATED EQUIPMENT operation manual and will regularly maintain the DEDICATED EQUIPMENT according to technical state of the art processes. Unless otherwise agreed upon in writing by the Parties in the PRODUCT SCHEDULE, BSP will conduct routine repairs, preventative and full maintenance, and calibration of the DEDICATED EQUIPMENT on its own expenses, at [***], as well as any extraordinary, corrective, or non-routine maintenance.

j. In case of termination of this AGREEMENT or any of its PRODUCT SCHEDULE, [***] shall bear the costs of decontamination and removal of the DEDICATED EQUIPMENT and shall be solely responsible for, and [***] shall have no liability whatsoever with respect to, the decommission, cleaning and decontamination of the DEDICATED EQUIPMENT in strict compliance with the APPLICABLE LAWS, including without limitation local health and safety requirements.

## 8. FORECAST.

1. [***] **Forecast**. Upon the execution of each PRODUCT SCHEDULE and in any event at the completion of the PPQ BATCHES, UGX shall provide BSP with the [***] forecast of the estimate of the quantities of DRUG PRODUCT that UGX expects BSP to MANUFACTURE during the [***] of the TERM for such DRUG PRODUCT for any dosage and any MANUFACTURING suite distributed [***] (the [***]] or [***]], as applicable, based on the expected DELIVERY DATE (such forecast, the "[***] FORECAST").

2. [***] **Forecast. Update**. On a [***] basis, on or before the [***] of the then applicable [***], UGX will provide BSP with a [***]-forecast for any dosage and any MANUFACTURING suite, which will be subsequently updated in accordance with the terms of this AGREEMENT, including without limitation Section 8.4 (each such forecast, a "[***] FORECAST").

**3.** **Binding Period**. Unless otherwise agreed by the Parties in any relevant PRODUCT SCHEDULE, each of such [***] FORECAST shall have:

1. the first [***]] periods corresponding to the first [***] of the first [***] of the [***] FORECAST, which will be binding on both Parties and expressed in requirements for [***] (the "BINDING FORECAST");

2. the remaining [***] corresponding to the last [***] of the [***] FORECAST, which will be non-binding on both Parties and thus provided for planning purposes only, except for a [***] that cannot be [***] per [***] that will be agreed by the Parties and included in the PRODUCT SCHEDULE; requirements for this period shall be expressed per [***].

3. From the EFFECTIVE DATE through the end of the [***], the quantities of DRUG PRODUCT requested by UGX will be supplied by BSP on the basis of PURCHASE ORDERS, subject to the terms and conditions of this AGREEMENT.

4. In the event that the assumptions on which this forecast mechanism is designed, such as the average of the [***] volumes and the limits set forth for the PERMISSIBLE FLUCTUATION, shall change, then the Parties shall meet and discuss in good faith the adjustments that shall be made to this forecast mechanism and its related flexibilities, which shall include obligations on long term capacity reservation for the [***] FORECAST and an extended BINDING FORECAST.

**4.** **Permissible Fluctuation.**

1. By the [***] day of [***] of any relevant [***], UGX will confirm to BSP the quantities of DRUG PRODUCT (expressed in number of BATCHES) that UGX intends to have delivered by BSP in the next succeeding BINDING PERIOD; such quantities shall be binding on both Parties and shall still be subject [***] and [***] to the [***], as set forth in the PRODUCT SCHEDULE, to be exercised during the BINDING PERIOD.

2. The PERMISSIBLE FLUCTUATION shall be exercised by UGX no later than [***] prior to the Delivery Date of the Product set forth in the BINDING FORECAST.

3. Notwithstanding anything of the foregoing, in the event that UGX wants that BSP manufactures a quantity of DRUG PRODUCT in excess of those identified in the BINDING FORECAST, then the Parties will discuss such UGX's request in good faith and BSP may agree, in its sole discretion, to PURCHASE ORDERS for the manufacture of such quantities of DRUG PRODUCT as it deems possible for it to manufacture in accordance with the terms of this AGREEMENT and with BSP's production plan.

5. [***] **and** [***]. Each PRODUCT SCHEDULE may contain (i) [[***] that BSP is [***] and UGX [***] in any [***] and (ii) a [***] with respect to the [***]. In the event that, for any reason whatsoever, [***] in excess of such [***] out of [***], the Parties shall [***]. The Parties shall discuss and agree in good faith [***]].

**6.** **Distribution of batches over the Binding Forecast.** Unless otherwise provided in this Agreement or in the PRODUCT SCHEDULE, the distribution of BATCHES over the BINDING FORECAST shall not [***]. In [***] of each [***], UGX and BSP shall [***] for the next succeeding BINDING FORECAST. UGX agrees to make [***] so that such [***] per [***] may not [***] over the [***] for the [***].

**7.** **Financial Obligations**. The financial obligations set forth in the BINDING FORECASTS shall be binding on both Parties in accordance with the terms of this AGREEMENT. In any event, if as of the end of each [***], UGX has not ordered for delivery in such [***] at least the aggregate quantity of DRUG PRODUCT set forth in the BINDING FORECAST ([***] through [***])] for such DRUG PRODUCT for such [***], then [***] the [***] set forth in [***] and those [***] at an amount equal to [***] ([***]%) of the [***]. Notwithstanding the foregoing, should [***] be able to [***] for UGX orders [***] [***], then only [***].

**8.** **PURCHASE ORDER.** UGXshall submit to BSP written PURCHASE ORDERS for MANUFACTURING SERVICES and ADDITIONAL SERVICES showing the content set forth in this Section 8.8. All DRUG PRODUCT ordered by UGX shall be in the form of a PURCHASE ORDER and , At least [***] prior to the DELIVERY DATE, UGX shall submit to BSP written PURCHASE ORDERS for DRUG PRODUCT to be provided by BSP, in accordance to the BINDING FORECAST. UGX shall specify in each PURCHASE ORDER, UGX's order number, the specific MANUFACTURING SERVICES and ADDITIONAL SERVICES being ordered, DRUG PRODUCT, quantity, MANUFACTURING SERVICE FEES, ADDITIONAL SERVICES fees, DELIVERY DATE and, to the extent applicable, milestones, deliverables, delivery schedule, payment schedule, invoicing address and other requirements. BSP shall, within [***] after the receipt of the PURCHASE ORDER accept in writing such PURCHASE ORDER. UGX shall be obligated to purchase, and BSP shall be obligated to have available for delivery on the DELIVERY DATE set forth in each PURCHASE ORDER, such quantities of DRUG PRODUCT as are set forth in such PURCHASE ORDER.

## 9. DELIVERY OF DRUG PRODUCT.

1. Any delivery of DRUG PRODUCT by BSP to UGX or to a THIRD-PARTY named by UGX will be based on [***] ([***]). BSP will package and ship DRUG PRODUCT along with the CERTIFICATE OF ANALYSIS and according to written instructions received from UGX for shipment in line with APPLICABLE LAWS and the QTA. In case UGX has special requirements for transport packaging, UGX shall inform BSP about such requirements in a timely manner. If agreed between the Parties such special packing requirements shall be documented in writing in a separate document between the Parties. Should BSP support UGX in performing activities associated with the shipment (i.e., without limitation, drafting and/or reviewing of transport documents, planning the delivery, contacting the designated carrier, etc.), an additional fee shall apply to these services that shall be mutually agreed upon by the Parties in the relevant PRODUCT SCHEDULE. UGX will supply to BSP, or bear all costs and expenses related with, the appropriate materials for packaging according to the specific requirements notified by UGX.

2. UGX may request in writing to BSP for a QUARANTINED SHIPMENT of BATCH of DRUG PRODUCT only in urgent cases and in accordance with BSP's internal procedures. QUARANTINED SHIPMENT shall be evaluated case by case by the Parties. Any and all BATCHES of DRUG PRODUCT sent in quarantine cannot be distributed on the market until UGX has received the CERTIFICATE OF ANALYSIS, proof of the full RELEASE. UGX assumes all risks, responsibilities and costs associated with a QUARANTINED SHIPMENT.

3. After RELEASE, BSP and UGX shall agree if (a) BSP shall place DRUG PRODUCT with a common carrier for delivery to UGX or a THIRD-PARTY, as directed by UGX and in accordance with Incoterms set forth in the Section 9.1, or (b) UGX shall pick up DRUG PRODUCT at the FACILITY, or (c) BSP shall store DRUG PRODUCT at the FACILITY within the limitations set forth in Section 9.5. and the fees detailed in the relevant PRODUCT SCHEDULE.

4. UGX will obtain, at its expense, any import license or other official authorization and carry out all customs formalities for the import of the goods and for their transport through any country. Where applicable, costs of customs formalities as well as all duties, taxes, and other charges payable upon export and anticipated by BSP will be recovered from UGX. Upon request, BSP shall assist UGX in [***] of import and export clearance and shall provide all relevant details or information requested by UGX in a timely manner throughout such process. Should BSP support UGX in performing activities associated with customs clearance formalities as well as all duties, taxes, and other charges payable upon export, [***] shall apply to these services. For sake of clarity, each [***] associated with the [***] shall be recovered from [***].

5. All DRUG PRODUCT at the FACILITY will be stored in a clean, secured, and segregated area under conditions according to DRUG PRODUCT SPECIFICATIONS and, to the extent applicable, the relevant PRODUCT SCHEDULE. UGX shall arrange for the pick-up of any DRUG PRODUCT within [***]CALENDAR DAYS of the DELIVERY DATE, which would be [***]. Should UGX not commit to such term BSP shall [***] ([***]) as set forth in the relevant PRODUCT SCHEDULE.

6. Upon BSP's request, BSP shall, at [***] costs and expenses and its sole discretion, ship, at the address included in the PRODUCT SCHEDULE within the timelines set forth in this Section 9.6, or destroy the (i) engineering (technical) BATCHES, if any, (ii) expired or NON-CONFORMING BATCHES, (iii) expired or non-conforming PURCHASED MATERIALS and/or FOC MATERIAL. Should UGX fail to notify its preference within [***]CALENDAR DAYS of the receipt of BSP's request, then BSP shall proceed with the return of such materials in accordance with the PRODUCT SCHEDULE, at [***]costs and expenses. UGX shall execute all relevant documentation necessary to export such materials in compliance with this AGREEMENT and APPLICABLE LAWS.

## 10. DRUG PRODUCT ACCEPTANCE AND REJECTION.

1. Each BATCH of DRUG PRODUCT will be sampled and tested by BSP against DRUG PRODUCT SPECIFICATIONS. The BSP's quality assurance will review the BATCH DOCUMENTATION for such BATCH and will assess if the MANUFACTURE has been performed in compliance with cGMP and the MANUFACTURING process. If, based upon such tests, a BATCH of DRUG PRODUCT conforms to the DRUG PRODUCT SPECIFICATIONS and was MANUFACTURED according to cGMP and the MANUFACTURING process, then a CERTIFICATE OF ANALYSIS will be completed and approved by BSP's qualified person for RELEASE. Complete and accurate BATCH DOCUMENTATION material for each BATCH of DRUG PRODUCT will be uploaded into a secured, password protected and dedicated electronic data room and with limited access to UGX. If UGX has not received all BATCH DOCUMENTATION and RECORDS within [***] BUSINESS DAYS after RELEASE as set forth in the QTA, UGX will promptly notify BSP in writing. If UGX requires additional copies of such BATCH DOCUMENTATION or RECORDS, these will be provided by BSP to UGX at [***] cost. UGX will review the BATCH DOCUMENTATION for each BATCH of DRUG PRODUCT and may test samples of such BATCH against the DRUG PRODUCT SPECIFICATIONS. During this review period, the Parties agree to respond promptly, in accordance with the QTA, to any reasonable inquiry by the other Party with respect to the BATCH DOCUMENTATION. UGX has no obligation to accept a BATCH or a portion of a BATCH, if such DRUG PRODUCT does not comply with the DRUG PRODUCT SPECIFICATION, the QTA, or was not MANUFACTURED in compliance with cGMP and with the MANUFACTURING process.

2. Upon receipt of any BATCH of DRUG PRODUCT, UGX, or its designee(s), shall inspect such BATCH of DRUG PRODUCT MANUFACTURED by BSP to ascertain that such BATCH of DRUG PRODUCT is free from physical defects at the incoming. Should a BATCH of DRUG PRODUCT have physical defects, UGX shall promptly inform BSP in writing and within [***] CALENDAR DAYS of the receipt of the affected BATCH of DRUG PRODUCT. Such written notice shall include the reason(s) for the rejection and to be accompanied with any supporting documentation or other evidence. A shipment of BATCH of

DRUG PRODUCT that is not rejected within the term of this Section 10.2 will be deemed accepted by UGX and the right to claim such defect shall be deemed waived by UGX, except if UGX discovers a LATENT DEFECT as set forth under Section 10.3 below.

3. If, after the RELEASE of a BATCH of DRUG PRODUCT by BSP, either Party discovers a LATENT DEFECT, such Party shall notify the other Party in writing within [***] BUSINESS DAYS after such LATENT DEFECT being detected or informed about by any of the Parties or their AFFILIATES, including THIRD PARTIES. THE RIGHT TO CLAIM A LATENT DEFECT SHALL BE DEEMED LOST IF EXERCISED IN RELATION TO A LATENT DEFECT [***].

4. In the event UGX notifies BSP, for any reason whatsoever, the rejection of any BATCH of DRUG PRODUCT within the timing set forth in this Article 10, the Parties shall run an investigation in accordance with the QTA.

5. BSP shall not be responsible for any NON-CONFORMING BATCH, unless to the extent BSP has caused it, as it results from the report of the investigation carried out in accordance with the QUALITY AGREEMENT. UGX will be responsible in any other event.

6. In the event that Parties are not in agreement to determine whether a BATCH is NON-CONFORMING or which Party is responsible for the NON-CONFORMING BATCH, the issue shall be submitted to a THIRD PARTY independent testing laboratory, jointly defined by the JOINT STEERING COMMITTEE, to perform any necessary tests and to review records, test data and other relevant information in order to ascertain conformity and/or responsibility. The THIRD PARTY independent laboratoryshall execute an appropriate confidentiality agreement approved in form and substance by BSP and UGX. Such THIRD PARTY'S decision shall be binding on both Parties. The costs of such THIRD PARTY independent laboratory shall be borne by the Party found to be at fault with respect to NON-CONFORMING BATCH.

7. Regardless of which Party is responsible for any NON-CONFORMING BATCH, unless otherwise advised by UGX, BSP will [***]to promptly MANUFACTURE and replace such NON-CONFORMING BATCH, and

10.7.1. If UGX is the Party responsible for such NON-CONFORMING BATCH, then UGX shall:

(i) pay for the NON-CONFORMING BATCH and such replacement DRUG PRODUCT on the [***] and at the [***]; and

(ii) bear the disposition costs of the NON-CONFORMING BATCH; and

(iii) have BSP MANUFACTURE the **r**eplacement DRUG PRODUCT, provided that UGX shall supply BSP with the sufficient quantity of FOC MATERIALS necessary to replace such NON-CONFORMING BATCH, at [***] costs and expenses.

10.7.2. Subject to Section 16, if BSP is the Party responsible for such NON-CONFORMING BATCH and UGX is willing to be supplied with a replacement DRUG PRODUCT BATCH, then, as sole remedies,

(a) to the extent UGX paid BSP for such NON-CONFORMING BATCH, BSP shall provide such a replacement BATCH of DRUG PRODUCT [***], or

(b) to the extent UGX did not pay BSP for such NON-CONFORMING DRUG PRODUCT, then UGX shall pay only for such a replacement DRUG PRODUCT BATCH on the [***] and at the [***] as for the [***], *provided that*

(c) in either case, UGX shall provide BSP with the sufficient quantity of FOC MATERIALS necessary to replace under (a) and (b) of this Section 10.7.2 such NON-CONFORMING BATCH, at [***] costs and expenses and BSP shall return or destroy, at [***] costs, the NON-CONFORMING BATCH as determined by UGX in its sole discretion.

(d) should UGX have (i) not opted for the replacement of NON –CONFORMING BATCH and (ii) [***] for such [***], [***] will [***] (or [***]if [***] under Section [***]) equal to [***], excluding [***]].With respect to [[***], [***]may [***] provided by [***] and, in the absence of [***] or[***] or in the event that the [***],[***] shall [***] the [***], excluding [***], within [***] CALENDAR DAYS after [***].

8. NOTWITHSTANDING ANYTHING TO THE CONTRARY IN THIS SECTION 10, BSP WILL [***], ONLY IF [***] WAS CAUSED BY [***] IN THE MANUFACTURING OF DRUG PRODUCT AND [***].

a. Notwithstanding the foregoing, UGX acknowledges that whether BSP is engaged for the performance of SERVICES, which involve scientific experiments requiring the use of reasonable judgment, any loss of API/DRUG SUBSTANCE in exercising such judgment shall not be regarded as loss due to [***]or [***].

b. Quality Control testing and analysis of any BATCH of DRUG PRODUCT MANUFACTURED by BSP shall be conducted by a THIRD PARTY independent laboratory engaged by UGX and approved by BSP. Any different setting regarding where to perform Quality Control testing and analysis of any BATCH of DRUG PRODUCT MANUFACTURED by BSP shall be discussed and agreed in good faith by the Parties being understood by the Parties that (i) BSP shall be preferred to any other THIRD-PARTY independent laboratory, provided BSP's Quality Control laboratories are considered by UGX to have sufficient technical capabilities and the economic offer submitted by BSP is comparable to other offers received by UGX, and (ii) in no event UGX shall negotiate and/or engage a THIRD PARTY that has competing business with BSP in the field of Drug Product contract manufacturing services.

c. After BSP has MANUFACTURED a minimum number of [***]successful commercial production BATCHES of DRUG PRODUCT for any single dosage and in the same MANUFACTURING suite, excluding PPQ BATCHES, the Parties will agree on the target yield for the DRUG PRODUCT (the "TARGET YIELD").

## 11. Price. Invoice and Payment.

1. UGX will pay to BSP the MANUFACTURING SERVICE FEE and ADDITIONAL SERVICES fee following the acceptance of an OFFER, which are set out in the PRODUCT SCHEDULE. The MANUFACTURING SERVICE FEE and ADDITIONAL SERVICES fee shall be subject to adjustment from time to time in accordance with this AGREEMENT; *provided that,* the MANUFACTURING SERVICE FEE and ADDITIONAL SERVICES fees may be amended based upon mutual agreement by the Parties.

2. The MANUFACTURING SERVICE FEE shall be adjusted pursuant to the provisions of this Section 11 and in any of the following events, upon agreement between the Parties in good faith:

1. [***];
2. [***];
3. [***], and
4. [***].

3. Effective as of [***] and at the beginning of each subsequent [***] during the TERM of this AGREEMENT, BSP shall be entitled to an adjustment to the MANUFACTURING SERVICE FEE and ADDITIONAL SERVICES fees, which adjustment shall be [***] in respect of [***] or [***] ([***]%)]. The adjusted MANUFACTURING SERVICE FEE and ADDITIONAL SERVICES fee shall be effective as of [***], in which the adjustment is requested and it will be notified by BSP on or about the first [***]of such relevant [***].

4. MANUFACTURING SERVICE FEE and ADDITIONAL SERVICES fee do not contain value-added tax (VAT). If MANUFACTURING SERVICES or ADDITIONAL SERVICES are subject to VAT, UGX will be charged for the VAT incurred in addition.

5. BSP will submit invoices to UGX upon RELEASE.Each invoice (i) must be submitted in compliance with any APPLICABLE LAWS and any specific requirements in this AGREEMENT and, (ii) will be accompanied by any information required by this AGREEMENT, including detailed information required for import purposes and for taxable amounts applicable to the MANUFACTURING SERVICE FEE and ADDITIONAL SERVICES fee.

6. All undisputed invoices will be paid within [***] CALENDAR DAYS from the receipt of BSP's electronic invoice, which is submitted to UGX's accounts payable department in compliance with the requirements of this AGREEMENT.

7. Except for [***] that are related to the MANUFACTURING process, UGX, in accordance with Section 9.6, shall be responsible for paying any costs related to [***] approved by UGX in accordance with this AGREEMENT.

8. Payment will be made in Euro, net of possible bank transfer fees and commissions imposed by UGX's sending bank, to the account designated by BSP.

9. Duty, sales, use or excise taxes imposed by any governmental entity that apply to the provision of MANUFACTURING SERVICES and ADDITIONAL SERVICES will be borne by [***](other than taxes based upon the income of BSP). Each Party shall therefore comply with its applicable taxation guidelines regarding filing and reporting for income tax purposes. Neither Party shall treat their relationship under this AGREEMENT as a partnership or as a pass-through entity for tax purposes.

## 12. Records. Audits and Inspections.

1. At its own expense, BSP will create and maintain accurate records related to the MANUFACTURING SERVICES, including, without limitation, reports, accounts, notes, data, and records of all information and results (collectively, the "RECORDS"). All RECORDS, to the extent they are specific to the DRUG PRODUCT and do not contain or incorporate BSP CONFIDENTIAL INFORMATION, BSP INVENTIONS or BSP's BACKGROUND INTELLECTUAL PROPERTY, will be the sole property of UGX, however, BSP shall have the right to retain one (1) copy of these DRUG PRODUCT-specific RECORDS to monitor compliance of this AGREEMENT, any of its PRODUCT SCHEDULE, QTA and APPLICABLE LAWS.

2. All original RECORDS of the development and MANUFACTURE of DRUG PRODUCT hereunder will be retained and archived by BSP in accordance with cGMP, APPLICABLE LAW and the QTA (the "RETENTION PERIOD"). In case of conflict the QTA shall prevail. Following the RETENTION PERIOD, BSP will not destroy the RECORDS without first giving UGX written notice and the opportunity to return the RECORDS at UGX's expense.

3. Upon the request of UGX, BSP shall permit to UGX to have access, during the TERM of this AGREEMENT (or, if applicable, after the TERM for activities started during the TERM but with effects after such TERM) to financial RECORDS limited to those related to the DRUG PRODUCT for the purpose of verifying the (i) compliance with the requirements of this AGREEMENT, including APPLICABLE LAW by BSP; (ii) the accuracy of any invoice submitted to UGX. For the avoidance of doubt, UGX or its designee may not have copies of such financial records but UGX shall be permitted to examine such records (during regular business hours) at such place or places where such financial records are customarily kept and maintained by BSP for the purpose of verifying the correctness of all such calculations invoiced by BSP hereunder. Upon request, BSP agrees to share with UGX in a secure password-protected digital data repository the certificate issued by a reputable accounting firm, which ascertains the accuracy of BSP's annual balance sheet, as well as the key financial data supporting BSP's independent auditor's report, provided that UGX shall keep such certificate strictly confidential with the prohibition of disclosure it to any third party without BSP's prior written consent.

4. UGX has the right to audit and inspect the FACILITY, equipment, materials and RECORDS as required by cGMP guidelines, this AGREEMENT and the QTA.

5. At reasonable times, upon reasonable advance written notice and subject to compliance with all applicable confidentiality provisions herein, UGX may request to perform cGMP audits at the FACILITY and BSP shall permit for such audits as outlined in the QTA. UGX and its duly authorized representatives may have access together with a BSP employee to the FACILITY, during operational hours and during active MANUFACTURING, to enter and inspect any premises and MANUFACTURING SERVICES and/or ADDITIONAL SERVICES to ascertain compliance by BSP with the terms of this AGREEMENT. BSP will cooperate with UGX to facilitate the evaluation and inspection, and provide reasonable assistance to UGX. UGX will reasonably cooperate with BSP to mitigate disruption to BSP's operations. Scope and further details are set forth in the QTA attached to Appendix III of this AGREEMENT. It is understood by the Parties that UGX may be accompanied by or delegate to THIRD PARTY's representatives the performance of such cGMP audits; provided that such THIRD PARTY's representatives shall (i) be bound by confidentiality obligations toward BSP no less stringent than those identified in this AGREEMENT and (ii) finalize a three-way confidentiality agreement which shall be accepted by all contracting parties.

6. UGX and/or its designees may perform *for-cause*audits as outlined in the QTA. BSP shall make the FACILITY and the relevant personnel involved in the performance of MANUFACTURING SERVICE and ADDITIONAL SERVICES under this AGREEMENT available, within reasonable business hours, for the purpose of any UGX audits.

7. BSP shall promptly inform UGX of any inspections by competent regulatory authorities at the FACILITY which affects the MANUFACTURE of DRUG PRODUCT under this AGREEMENT, within the terms provided in the QTA. In the event that the inspection reveals that BSP is not in compliance with the APPLICABLE LAWS and applicable regulatory regulations, including cGMP, and receives written observations (or any other written communication) by such REGULATORY AUTHORITY which involve the DRUG PRODUCT, BSP shall (i) use its best efforts to cure such non-compliance within the timing required by the REGULATORY AUTHORITY at [***] costs and expenses, (ii) inform UGX of any proposed written response by BSP to any such inspection, and (iii) provide UGX with copies of all documentation within the terms provided in the QTA. UGX will have the opportunity to review and provide input to the response to BSP as promptly as practicable and in accordance with the QTA.

8. BSP agrees that, at UGX's option, up to [***]PERSONS IN PLANT may be present at the FACILITY during the MANUFACTURING for the purposes of check weighing and documenting MANUFACTURING and all associated RECORDS in connection therewith. Any PERSON IN PLANT who are present at the FACILITY, shall comply with BSP's site regulations, SOPs and rules.

## 13. Intellectual Property.

a. Neither Party shall, as a result of this AGREEMENT, acquire any right, title, or interest in any INTELLECTUAL PROPERTY RIGHTS that the other Party owns or controls as of the EFFECTIVE DATE of this AGREEMENT, or that the other Party obtains ownership or control of separately and apart from the performance of the MANUFACTURING SERVICES and ADDITIONAL SERVICES under this AGREEMENT and without the use of the other Party's Confidential Information ("BACKGROUND INTELLECTUAL PROPERTY").

b. For the TERM, UGX hereby grants to BSP, a limited, non-exclusive, fully paid-up, royalty-free, non-transferable license to use UGX BACKGROUND INTELLECTUAL PROPERTY related to the DRUG PRODUCT that BSP is required to use in order to perform the SERVICES (as specified in the PRODUCT SCHEDULE) solely for the purpose of this AGREEMENT.

c. UGX shall own exclusively all rights, titles, and interests in any and all INVENTIONS directly related to the DRUG PRODUCT, MANUFACTURE of DRUG PRODUCT or UGX's BACKGROUND INTELLECTUAL PROPERTY and which result from use of UGX's CONFIDENTIAL INFORMATION and/or FOC MATERIALS, but excluding BSP INVENTIONS and BSP's BACKGROUND INTELLECTUAL PROPERTY (collectively, "UGX INVENTIONS"). BSP hereby assigns, and commits to assign, all right, title and interest in to UGX INVENTIONS to UGX

d. Notwithstanding the foregoing, BSP shall own all rights, titles and interests in any BSP INVENTIONSand UGX hereby assigns all right, title and interest in BSP INVENTIONS to BSP. As used herein, "BSP INVENTIONS" means any IMPROVEMENTS to BSP'sBACKGROUND INTELLECTUAL PROPERTY developed, conceived, invented, reduced to practice or made solely by BSP in the course of performance of the MANUFACTURING SERVICES and ADDITIONAL SERVICES, which relate to BSP's line of business or the way BSP performs its services, and which do not use or include any UGX's BACKGROUND INTELLECTUAL PROPERTY, UGX INVENTIONS and UGX's CONFIDENTIAL INFORMATION or any other property of UGX.

e. BSP commits to promptly inform UGX according to section 23.4 (NOTICE SECTION) of any violation of UGX's BACKGROUND INTELLECTUAL PROPERTY and UGX INVENTIONS and further agrees, at UGX`s expense, to (i) assist UGX or its designee(s) under APPLICABLE LAWs, in obtaining, maintaining, defending and enforcing patents and all other instruments in nature of patents with respect to any UGX's BACKGROUND INTELLECTUAL PROPERTY and UGX INVENTIONS, (ii) provide assistance and execute such documents as UGX or its designee(s) may request from time to time, and (iii) confirm the assignments hereunder. For clarity, UGX or its designee(s) shall be the only Party responsible for filing, prosecuting and maintaining any patent application covering UGX INVENTIONS and UGX's BACKGROUND INTELLECTUAL PROPERTY

f. BSP hereby grants to UGX a perpetual, non-exclusive, nontransferable, royalty-free, fully paid-up, worldwide rights to use any and all of BSP INVENTIONS solely for the development, MANUFACTURING, formulation, packaging, importation, use, marketing, distribution and sale of DRUG PRODUCT, unless expressly otherwise agreed upon by the Parties. Such rights shall be sublicensable by UGX to its AFFILIATES, licensees or collaboration partners only for the same limited purposes set forth in this Section 13.6, provided that (i) UGX has promptly notified BSP in writing about such sublicense, and (ii) the AFFILIATE, licensee or collaboration partner has first agreed in writing to maintain BSP INVENTIONS in confidence throughout a confidentiality agreement among the Parties and such AFFILIATE, licensee or collaboration partner.

g. BSP will not knowingly utilize in the performance of the MANUFACTURING SERVICES and ADDITIONAL SERVICES under a PRODUCT SCHEDULE or incorporate into the DRUG PRODUCT or INVENTIONS any proprietary rights of a THIRD PARTY except as BSP is permitted to do it without further compensation by UGX to BSP or any other THIRD PARTY. If the performance of this AGREEMENT requires the use of IP RIGHTS of a THIRD-PARTY, UGX hereby grants to or procures for BSP the necessary rights of use to these IP RIGHTS solely for the performance of the MANUFACTURING SERVICES and ADDITIONAL SERVICES and provided that the Parties enter in a license agreement with such THIRD PARTY to regulate the use of IP RIGHTS of THIRD-PARTY.

h. All documents that BSP receives from UGX for the fulfillment of the MANUFACTURING SERVICES and ADDITIONAL SERVICES, which contain UGX CONFIDENTIAL INFORMATION, UGX INVENTIONS or UGX BACKGROUND INTELLECTUAL PROPERTY, shall remain the property of UGX.

i. Each Party shall be obliged to acquire the INVENTIONS and rights on the respective BACKGROUND INTELLECTUAL PROPERTIES, as applicable, made under this AGREEMENT of its employees, consultants, agents and representatives to the extent necessary to secure the other Party's rights set out in this section.

## 1. Indemnification.

a. EachParty shall indemnify, defend and hold the other Party and its AFFILIATES, officers, employees and agents (collectively the "INDEMNITEES" and each an "INDEMNITEE") harmless from and against any and all losses, costs, damages, fees or expenses ("LOSSES") incurred and suffered by a Party's INDEMINITEE in connection with or arising out of any THIRD-PARTY claims, demands, suits, proceedings or causes of actions ("CLAIM") to the extent arising out of:

1. the material breach by such Party of the provisions of this AGREEMENT, including any covenants, representations and warranties set forth herein;
2. the gross negligence or willful misconduct of such Party in the performance of any obligations under this AGREEMENT;
3. the infringement or misappropriation of the IP RIGHTS of a THIRD PARTY in connection with the use by a PARTY of the other Party's IP rights.

With respect to each Party, the indemnification obligations set forth in this Section 14.1 shall not apply to the extent that the LOSSES are the result of (i) a material breach of this AGREEMENT (including a breach of any representation, warranty or covenant) by the other Party, or (ii) the [***] of the other Party's INDEMNITEES, or (iii) for which the other Party is obligated to [***] as set forth in Sections [***], [***] and [***] below].

b. A Party seeking indemnification under this Section 14 (the "INDEMNIFIED PARTY")in respect of a THIRD PARTY CLAIM, shall give to the other Party from which recovery is sought (the "INDEMNIFYING PARTY") prompt written notice of any LOSSES or the discovery of any fact upon which the INDEMNITEE(S) intends to base an indemnification request pursuant to section 14.1 ("INDEMNIFICATION NOTE"); provided, however, that failure to give such INDEMNIFICATION NOTE will not relieve the INDEMNIFYING PARTY of its obligations under this Article 14 except to the extent that INDEMNIFYING PARTY is materially prejudiced by such failure. Each INDEMNIFICATION NOTE must contain a description of the CLAIM and the nature and the amount of such LOSS (to the extent that the nature and the amount are known at such time). Together with the INDEMNIFICATION NOTE, the INDEMNIFIED PARTY shall

furnish promptly to the INDEMNIFYING PARTY copies of all the notices and documents (including court papers) received by the INDEMNITEE(S) in connection with CLAIM. The INDEMNIFYING PARTY shall not be obligated to indemnify the INDEMNITEE to the extent any admission or statement made by the INDEMNITEE materially prejudices the defense of such CLAIM. If practicable, the INDEMNIFYING PARTY shall promptly send a copy of the INDEMNIFICATION NOTE to its relevant insurers and shall permit them to exercise rights of subrogation, if it is permitted by APPLICABLE LAW.

c. Without limiting the foregoing, at its option the INDEMNIFYING PARTY may assume control of the defense of any such CLAIM by giving written notice to the INDEMNIFIED PARTY within [***] CALENDAR DAYS after the receipt of an INDEMNIFICATION NOTE by INDEMNIFIED PARTY. The INDEMNIFYING PARTY will have the right to solely defend the THIRD-PARTY CLAIM; provided, however, that such settlement does not adversely affect the INDEMNIFIED PARTY's rights or obligations hereunder or admit liability on INDEMNIFIED PARTY's part. The INDEMNIFYING PARTY agrees not to enter into any settlement which would have a material adverse effect on the INDEMNITEE(S) without prior to the written consent of the INDEMNITEE(S), which consent shall not be unreasonably withheld. The INDEMNIFIED PARTY and/or any relevant INDEMNITEE will reasonably cooperate with the INDEMNIFYING PARTY and its legal representatives in the investigation and defense of any THIRD-PARTY CLAIM and may choose, in their sole discretion, to be represented by counsel of its own selection and at its own expense in or with respect to any such THIRD-PARTY CLAIM. The indemnification under this ARTICLE 14 shall not apply to amounts paid with respect to settlement of any THIRD-PARTY CLAIM if such settlement is effected without the prior written consent of THE INDEMNIFYING PARTY, which consent will not be unreasonably withheld or delayed.

d. If the INDEMNIFYING PARTY chooses not to take control of the defense or prosecute any CLAIM, the INDEMNIFIED PARTY shall retain control of the defense thereof, but no INDEMNIFIED PARTY or INDEMNITEE(S) shall admit any liability with respect to, or settle, compromise or discharge, any such CLAIM without the prior written consent of the INDEMNIFYING PARTY, which consent shall not be unreasonably withheld or delayed.

## 1. General Representation and Warranties.

a. Each Party represents and warrants to the other Party that:

i. It is a corporation duly organized, validly existing and in good standing under the laws and regulations of the state in which it is incorporated.

ii. It has the corporate power and authority and the legal right to enter into this AGREEMENT and any and all of this Annexes and to perform its obligations hereunder.

iii. This AGREEMENT, when executed and delivered by such Party in accordance with the provisions hereof, will be a legal, valid and binding obligation of such Party, enforceable against such Party in accordance with its terms, except as such enforceability may be limited by applicable bankruptcy, insolvency, moratorium, reorganization or similar laws affecting the enforcement of creditors' rights generally and by general principles of equity.

iv. No contract, agreement, promise, undertaking or other fact or circumstance prevent the performance of the obligations under this AGREEMENT.

v. The execution and delivery of this AGREEMENT and the performance of the Party's obligations hereunder do not conflict with or violate any requirement of APPLICABLE LAWS, and do not conflict with, or constitute a default under, any contractual obligation of such Party.

vi. At the EFFECTIVE DATE, itself, its directors, officers or employees have not offered, promised, given, authorized, solicited or accepted an undue pecuniary or other advantage of any kind (or implied that they will or might do any such thing at any time in the future) in any way connected with the AGREEMENT and that it

has taken reasonable measures to prevent subcontractors, agents or any other third parties, subject to its control or determine influence, from doing so in accordance to any APPLICABLE LAW.

**b. BSP's Representations and Warranties.** In addition to the provision of Section 15.1., BSP represents and warrants that:

1. The MANUFACTURING SERVICES and ADDITIONAL SERVICES will be performed in a safe and ethical manner with requisite care, skill and diligence, in accordance with the APPLICABLE LAWS, industry standards and this AGREEMENT, and by individuals who are appropriately trained and qualified.
2. the DRUG PRODUCT MANUFACTURED under this AGREEMENT (including all MANUFACTURING SERVICES and BSP's employment practices) complies with cGMP (if applicable), the MANUFACTURING process, the QTA and DRUG PRODUCT SPECIFICATIONS, and (ii) will not be adulterated or misbranded under the United States Federal Food, Drug and Cosmetic Act (the "FDCA") or all APPLICABLE LAW.
3. BSP has obtained all permits, licenses and other authorizations, which are required under APPLICABLE LAW to MANUFACTURE and deliver the DRUG PRODUCT. BSP is in compliance with, and during the TERM of this AGREEMENT will take all actions necessary to comply, with all terms and conditions of any and all required permits, licenses and authorizations applicable to the MANUFACTURE and supply of DRUG PRODUCT.
4. BSP shall not subcontract any performance of this AGREEMENT to any other THIRD PARTY without UGX's prior written consent.
5. The DRUG PRODUCT is free from defects in material and workmanship.
6. The DRUG PRODUCT is free from all liens, CLAIMS and encumbrances.
7. BSP has the right to make any grants of BSP INVENTION that it makes or is required to make under Section 13.6 of this AGREEMENT.
8. To the best of BSP's knowledge, the DRUG PRODUCT does not infringe any INTELLECTUAL PROPERTY RIGHTS of any other THIRD PARTY, and any use thereof by UGX consistent with this AGREEMENT does not infringe such rights.
9. it does not and shall not employ, contract with or retain any person directly or indirectly to perform MANUFACTURING SERVICES and/or ADDITIONAL SERVICES Services under this AGREEMENT if such person is debarred under 21 U.S.C. 335a (a) or (b) or, if agreed by the Parties, other equivalent laws, rules, regulations or standards of any other relevant jurisdiction.

**c. UGX's Representations and Warranties.** In addition to the provision of Section 15.1, UGX represents and warrants that:

1. All FOC MATERIALS provided to BSP conform and will conform to the FOC MATERIALS SPECIFICATIONS and such FOC MATERIALS have been manufactured in compliance with applicable cGMP and all APPLICABLE LAWS and shall not be adulterated at any time prior to delivery to BSP.
2. UGX has the right to make any grants of UGX INTELLECTUAL PROPERTY RIGHTS to the DRUG PRODUCT(S) it makes or is required to make under the AGREEMENT.
3. To the best of UGX's knowledge, the DRUGPRODUCT(S) and deliverables do not infringe any INTELLECTUAL PROPERTY RIGHTS of any other THIRD PARTY, and any use thereof by BSP consistent with this AGREEMENT does not infringe such rights.
4. Neither UGX nor any other THIRD PARTY who performs any obligation of UGX under the AGREEMENT is prohibited from doing so by any: (i) APPLICABLE LAW; (ii) covenant not to compete;(iii) contract to deal exclusively with another THIRD PARTY; or (iv) other legal or professional obligation or restriction.
5. The performance of UGX's responsibilities under the AGREEMENTand UGX's use of the MANUFACURING SERVICES and DRUGPRODUCT comply with all APPLICABLE LAW.

**d. Disclaimer of Warranties.** EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY MAKES NO WARRANTY OF ANY KIND, EITHER EXPRESSED OR IMPLIED, BY FACT OR LAW, OTHER THAN THOSE EXPRESSLY SET

FORTH IN THIS AGREEMENT, INCLUDING, BUT NOT LIMITED TO, WARRANTY OF FITNESS FOR A PARTICULAR PURPOSE OR WARRANTY OF MERCHANTABILITY OR NON-INFRINGEMENT.

## 1. Limitation of Liability.

a. Subject to Section 16.2 and except for those obligations of BSP under Section 10, as sole remedy for UGX, in case of replacement of Non-Conforming BATCH for BSP's fault, BSP's maximum annual liability under this AGREEMENT for any reason whatsoever resulting from a breach of its representations, warranties or other obligations under this AGREEMENT shall not exceed [***] pursuant to Section [***].

b. The limitation under this Section 16 does not apply in case of liability arising out of [***], [***]or [***] of or [***] and [***] under Section[***] by any of the Party.

c. EACH PARTY EXCLUDES ANY LIABILITY FOR SPECIAL, INDIRECT, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE AND EXEMPLARY DAMAGES, RECALL COSTS, LOSS OF PROFIT ARISING OUT OF OR RELATED TO THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, HOWEVER CAUSED, PROVIDED THAT SUCH DAMAGES HAVE NOT BEEN CAUSED BY THE OTHER PARTY'S [***] OR [***], BREACH OF [***] AND [***] IN SECTION [***] OR [***] PURSUANT TO SECTION [***].

d. If BSP's cooperation is required in administrative procedures, especially in procedures of admission, customs or of importation, UGX indemnifies BSP from any liability which may arise out of this cooperation, except to the extent arising from BSP`s [***]or [***].

## 1. Insurance.

1. Either Party shall, at its sole cost and expense, obtain and maintain in force for the TERM of the AGREEMENT and for [***] triggered in compliance with Section 20, adequate and suitable insurance in the minimum amounts set forth below with a reputable insurance company to cover its liability under this AGREEMENT.

2. UGX will maintain a comprehensive product liability insurance, with combined single limits of [***] USD for each claim with respect to personal injury and/or damage to property and [***] USD aggregate.

3. BSP will maintain comprehensive/general liability insurance coverage to include BSP's liability, with respect to MANUFACTURING SERVICES and ADDITIONAL SERVICES toward UGX, with combined single limits of [***] USD for each claim with respect to personal injury and/or damage to property and [***]USD in aggregate.

4. For the avoidance of any doubt, each Party is allowed to change the insurer anytime, *provided that* all the conditions described in this Section 17 are properly met.

5. Upon UGX's request, BSP will provide UGX with a certificate of insurance evidencing the insurance coverage specified in this section.

6. BSP shall not maintain specific insurance coverage for the FOC MATERIALS, which insurance coverage shall be obtained by UGX. For the sake of clarity, notwithstanding the foregoing, such FOC MATERIALS while in the care, custody and control of BSP shall remain covered under [***] policy.

## 2. Confidential Information.

a. CONFIDENTIAL INFORMATION means any and all confidential and proprietary information of the Parties, which is not included in the exceptions set forth in Section 18.4, and whether disclosed in oral, written, visual, electronic or

other forms, and which either Party or its personnel observes or learns in connection with this AGREEMENT or any SERVICES performed hereunder, or in negotiation of this AGREEMENT. Confidential information may also include without limitation: (i) business plans, strategies, forecasts, projects and analyses, results, records, either Party's BACKGROUND INTELLECTUAL PROPERTY, UGX INVENTIONS, BSP INVENTIONS generated under this AGREEMENT; (ii) financial information, fee structures and pricing; (iii) business processes, methods and models; (iv) personnel and supplier information; (v) deliverables and work DRUG PRODUCT; (vi) DRUG PRODUCT, service specifications,MANUFACTURING or professional services proposals and other information relating to MANUFACTURING capabilities and operation; (vii) MANUFACTURING, purchasing, logistics, sales and marketing information; (viii) the terms and conditions of this AGREEMENT and (ix) personally identifiable information as to any individual involved in the provision of MANUFACTURING SERVICES and ADDITIONAL SERVICES, including medical or religious status or preference and their nationality (collectively "CONFIDENTIAL INFORMATION"). Each Party acknowledges the confidential, proprietary, and secret character of the CONFIDENTIAL INFORMATION. Additionally, either Party agrees to keep any CONFIDENTIAL INFORMATION subject to the same use and disclosure limitations, as set forth in this Section 18 during the TERM of this AGREEMENT and for [***] years following termination or expiration thereof.

b. Each of the Parties will keep the CONFIDENTIAL INFORMATION of the respective other Party secret. Parties will use the CONFIDENTIAL INFORMATION only for the purposes of performing SERVICES, obligations and exercising rights under this AGREEMENT and not disclose such CONFIDENTIAL INFORMATION to any THIRD-PARTY without the prior consent of the other Party.

c. Each Party shall limit the disclosure of the otherParty's CONFIDENTIAL INFORMATION to its AFFILIATES, officers, employees , who reasonably require to access to such CONFIDENTIAL INFORMATION on a need-to-know basis and only for the purpose to performMANUFACTURING SERVICES and ADDITIONAL SERVICES under this AGREEMENT The receiving Party will use its reasonable efforts to ensure that any AFFILIATE, employee or officer to which it discloses CONFIDENTIAL INFORMATION will be under confidentiality and non-use obligations as stringent as those contained herein.

d. The provisions of this Section 18 do not apply to information which receiving Party proves that:

1. the receiving Party already knew at the time of disclosure, other than by breach of this AGREEMENT by the receiving Party; or
2. is or becomes public knowledge after disclosure by the disclosing Party, other than through the receiving Party's breach of this AGREEMENT; or
3. the receiving Party receives in good faith from a THIRD-PARTY not in violationof an obligation of confidentiality toward the disclosing Party; or
4. the receiving Party independently develops or discovers the information without use of or reference to the Confidential Information of disclosing Party, as evidenced by receiving Party's written records.

e. For the avoidance of doubt, no provision in this AGREEMENT shall restrict each Party's right to disclose the existence of a business relationship between the Parties to potential other customers, provide that the affected Party shall require the prior written consent of the other Party before any of such disclosure and the consent will not be unreasonably withheld or delayed.

f. Notwithstanding anything herein to the contrary, each receiving Party may disclose the Confidential Information to the extent it is legally compelled to disclose it, provided, however, that prior to any such compelled disclosure, the receiving Party shall give the disclosing Party reasonable advance notice of any such disclosure and shall cooperate in protecting against the disclosure and/or obtaining a protective order narrowing the scope of such disclosure of the CONFIDENTIAL INFORMATION.

g. Each Party may retain one (1) copy of CONFIDENTIAL INFORMATION, and use this archive copy to comply with the APPLICABLE LAW, and tax law provisions and to ensure and verify the continued compliance with the obligations undertaken hereunder.

h. Notwithstanding anything to the contrary in this AGREEMENT, upon written request of the disclosing Party, the receiving Party shall return to the disclosing Party or destroy, at disclosing Party sole option and expenses, all CONFIDENTIAL INFORMATION, together with copies thereof, *provided that* the disclosing Party shall not require the receiving Party to destroy or return the CONFIDENTIAL INFORMATION stored securely by receiving Party during automatic system back-up in accordance with receiving Party's internal IT procedures.

## 3. Force Majeure.

1. Except for due payment obligations, neither Party is liable to the other Party for failure or delay in performing its obligations under this AGREEMENT to the extent and for so long as such failure or delay results from causes beyond the reasonable control of such Party including fires, earthquakes, floods, natural disasters, embargoes, wars, acts of war (whether war is declared or not), terrorist acts, insurrections, riots, civil commotion, strikes, lockouts, epimedics/pandemics, or other labor disturbances, acts of God or government acts, sabotage and acts of terrorism, cyberattacks, lack of or inability to obtain sufficient fuel, power or components, materials, labor containers, interruption of or delay in transportation, supplies or defective equipment, breakage or failure of machinery or apparatus, excluding breakage for lack of or inadequate maintenance (each, a "FORCE MAJEURE EVENT"). In the event of the occurrence of FORCE MAJEURE EVENT, each Party must promptly notify the other Party and will use its [***] to avoid, mitigate or remove the FORCE MAJEURE EVENT. Notwithstanding the foregoing, should UGX have technical difficulties to authorize or release the payments to BSP to fulfill its obligations due to a FORCE MAJEURE EVENT, the Parties shall meet in good faith and use their best efforts to set up a payment plan.

2. Such excuse shall continue as long as the FORCE MAJEURE EVENT continues, provided that, upon cessation of such FORCE MAJEURE EVENT, the affected Party shall promptly resume its performance and obligation hereunder. If the Party is unable to resume its performance and obligation under this AGREEMENT, such Party shall prompt notify the other Party of its inability and the Parties shall meet promptly to determine an equitable solution to the effects of any such FORCE MAJEURE EVENT.

## 4. Term and Termination.

a. Term. This AGREEMENT effectiveness starts with the EFFECTIVE DATE and will expire, if not terminated earlier in accordance with this Section 20, [***]) CALENDAR YEARS thereafter] ("TERM"). This AGREEMENT will be automatically extended for another [***]-year period following the first [***] TERM (each, a "RENEWAL TERM"), unless a Party provides written termination notice of its intent to not renew the AGREEMENT at least [***] CALENDAR MONTHS prior to the expiry of the initial TERM or any further RENEWAL TERM. If this AGREEMENT is terminated in its entirety, then all PRODUCT SCHEDULE also will terminate. The termination of one PRODUCT SCHEDULE shall not affect any other PRODUCT SCHEDULE or the AGREEMENT.

b. Termination.In addition to any other provision of this AGREEMENT or a PRODUCT SCHEDULE expressly providing for termination of this AGREEMENT or such PRODUCT SCHEDULE, this AGREEMENT or a PRODUCT SCHEDULE may be terminated as follows:

a. This AGREEMENT or a PRODUCT SCHEDULE might be terminated by either Party without cause with [***] CALENDAR MONTHS' notice period for termination to the other Party.

b. Each Party shall be entitled to terminate this AGREEMENT with immediate effect if:

i. any obligation provided in this AGREEMENT or PRODUCT SCHEDULE is materially breached by the respective other Party and/or its AFFILIATES and is not cured or attempted to cure within [***]CALENDAR DAYS of written notice thereof;

ii. MATERIAL CHANGE in CONTROL of the respective other Party which affects such Party`s ability to fulfill its contractual obligations hereunder. In such event, the affected Party will have the one-time right, exercisable

within [***] calendar days after such MATERIAL CHANGE in CONTROL, to terminate this Agreement upon prior written notice to the non-affected Party.

c. UGX shall be entitled to terminate this AGREEMENT with immediate effect if BSP fails to maintain the necessary rights, permits and approvals to perform the SERVICE under this AGREEMENT.

d. UGX may terminate this AGREEMENT in its entirety or any relevant PRODUCT SCHEDULE with immediate effect, at UGX's option, in case UGX fails to obtain the regulatory approval of the DRUG PRODUCT from any health authority globally. In case of termination pursuant to this Section 20.2.4, UGX shall compensate BSP only for [***], determined pursuant to Section [***], and those [***] at an amount equal to [***] of the [***].

e. Either Party may terminate in the event for FORCE MAJEURE EVENT lasting longer than [***] consecutive [***] as provided in Section 19.

f. Either Party may terminate this AGREEMENT in its with immediate effect in accordance with the provisions of Section 23.5.

g. If a Party becomes bankrupt, makes an assignment for the benefit of creditors, or has a trustee appointed for all or substantially all of that Party's property, or if any case or proceeding will have been commenced or other action taken by or against that Party in bankruptcy or seeking reorganization, liquidation, dissolution, winding-up, arrangement, composition or readjustment of its debts or any other relief under any bankruptcy, insolvency or reorganization or other similar act of law of any jurisdiction now or hereafter in effect (any such event or proceeding, a "BANKRUPTCY"), the other Party will have the right to terminate this AGREEMENT and/or any PRODUCT SCHEDULE hereto immediately upon prior written notice to the Party in BANKRUPTCY.

c. **Ban, Withdrawal, Discontinuation of Products.**

1. If (i) any DRUG PRODUCT is withdrawn by a REGULATORY AUTHORITY, or (ii) UGX withdraws any DRUG PRODUCT voluntarily from the market in all countries, UGX must notify BSP to immediately cease MANUFACTURE of the applicable DRUG PRODUCT.

2. If UGX requests cessation of MANUFACTURE of a DRUG PRODUCT in connection with the occurrence of an event described in Section 20.3.1 that is not due to BSP's fault to comply with the provisions of this AGREEMENT and the relevant PRODUCT SCHEDULE, UGX shall pay BSP an amount equal to [***]% of the SERVICE FEE of such cancelled quantities of DRUG PRODUCT as set forth in the BINDING FORECAST. Alternatively, if applicable, UGX may request that BSP MANUFACTURES [***] In such a case, the Parties shall meet either in person or by teleconference and discuss in good faith the terms of the transfer, the equivalence and compensation with respect to the non-absorbed capacity. Notwithstanding anything of the foregoing, should BSP be [***] by using its [***] and to the extent consistent with BSP's obligations [***], then [***].

d. If UGX elects to MANUFACTURE a DRUG PRODUCT, or to have a DRUG PRODUCT MANUFACTURED by another manufacturer, BSP will provide [***] to assist UGX with all activities necessary to allow UGX to complete a technical transfer of MANUFACTURING of DRUG PRODUCT from BSP to UGX or to such an alternative manufacturer selected by UGX ("TRANSFER REQUEST"). BSP will cooperate in transferring and provide UGX with a full inventory of all FOC MATERIALS and PURCHASED MATERIALS related to the concerned DRUG PRODUCT, together with all data documentation and all other information that BSP generated as part of providing MANUFACTURING SERVICES and ADDITIONAL SERVICES to UGX and which are necessary in order to complete the TRANSFER REQUEST, excluding BSP's BACKGROUND INTELLECTUAL PROPERTY and BSP INVENTIONS. BSP shall not be obligated to permit personnel from any other THIRD PARTY, whether or not such THIRD PARTY is a BSP's competitor, to enter the FACILITY, nor shall any BSP's CONFIDENTIAL INFORMATION, BSP's BACKGROUND INTELLECTUAL PROPERTY and BSP INVENTIONS be shared with such THIRD PARTY, without having in place a three-way confidentiality agreement accepted by the concerned Parties and, in any event, the prior written consent of BSP.

e. Survival. The following Articles and Sections shall survive the termination or expiration of this AGREEMENT for any reason: 11 (Price. Invoice and Payment), 12. 1 and 12.2 (Records), 13 (Intellectual Property), 14 (Indemnification),

15(General Representations and Warranties), 16 (Limitation of Liability), 17 (Insurance), 18 (Confidential Information), 20 (Term and Termination), 21 (Decomissioning), 22 (Effects of Termination), 23 (Miscellaneous) and 20.5 (Survival)**.**

## 5. Decommissioning.

1. Upon expiration or termination of this AGREEMENT or of a PRODUCT SCHEDULE for any reason, unless otherwise provided in this Section 21, each Party will promptly perform the DECOMMISSIONING actions set forth in this Section 21, taking into account that such actions may be delayed to the extent necessary for such Party to fulfill any outstanding MANUFACTURING SERVICES and/or ADDITIONAL SERVICES or PURCHASE ORDERS as of the date of such expiration or termination. In accordance with the provisions of this Section 21 and upon the written request of a Party, BSP and UGX will take the following actions with respect to the applicable PRODUCT SCHEDULE:

1. BSP ceases and refrains from MANUFACTURING and supplying DRUG PRODUCT for UGX.
2. The receiving Party shall deliver to disclosing Party all disclosing Party`s CONFIDENTIAL INFORMATION, BACKGROUND INTELLECTUAL PROPERTY, INVENTIONS, Records containing or comprising the disclosing Party's CONFIDENTIAL INFORMATION that the receiving Party has maintained under this AGREEMENT. Notwithstanding the foregoing, (i) the receiving Party may retain and continue to use copies of such data, Records, and documentation as required to comply with all APPLICABLE LAWS, and (ii) BSP legal department may retain one copy of the foregoing, in each case, subject to its continuing obligation of the confidentiality under Section 16.
3. BSP shall return to UGX all remaining DRUG PRODUCT, WORK IN PROCESS and FOC MATERIALS in BSP's possession or destroy such FOC MATERIALS, DRUG PRODUCT and WORK IN PROCESS as determined in UGX's sole discretion and cost as set forth in Section 22.3.

2. Prior to commencing DECOMMISSIONING and during the period of any DECOMMISSIONING, the JOINT WORKING TEAM will meet and discuss in good faith and agree upon a plan for such DECOMMISSIONING.

## 6. Effects of Termination.

1. Expiration or termination of this AGREEMENT or a PRODUCT SCHEDULE for any reason shall not exempt any Party from paying to any other Party any undisputed amounts owed to such Party at the time of such expiration or termination. Notwithstanding the foregoing, neither BSP nor UGX shall have any further obligations under this AGREEMENT or a PRODUCT SCHEDULE, as applicable, except as set forth in this Section 22. In case of termination, together with the notice UGX shall notify BSP of its intention or not to have the DRUG PRODUCT MANUFACTURED as identified in the BINDING FORECAST and as determined pursuant to Section 8.

1. Should UGX request BSP to MANUFACTURE the DRUG PRODUCT forecasted pursuant to Section 8, then the MANUFACTURING SERVICES and/or ADDITIONAL SERVICES shall be run as usual and BSP shall be compensated for the quantities set forth in the BINDING FORECAST in accordance with the terms of this Agreement.

2. In the event UGX notifies BSP of its intention to terminate this AGREEMENT or any PRODUCT SCHEDULE and not to have DRUG PRODUCT MANUFACTURED during the [***] period after the termination notice, then UGX shall be bound to pay to BSP [***] of the quantities set forth in the BINDING FORECAST, *provided that* this payment obligation of UGX shall not apply in case this AGREEMENT or any PRODUCT SCHEDULE is terminated by UGX pursuant to Section 20.2.7 (termination for insolvency) or Section 20.2.2 (a)(uncured material breach). Notwithstanding anything of the foregoing, should BSP be able to reallocate the unused reserved capacity for UGX orders to other clients' business opportunities by [***] and to the extent consistent with [***], then the amount resulting from the difference between the amount due for the order(s) cancelled by UGX and the amount recovered by BSP shall be [***].

3. Alternatively, if applicable, UGX may request that BSP MANUFACTURE one or more DRUG PRODUCT(s) other than the discontinued DRUG PRODUCT in order to fill, in whole or in part, the MANUFACTURING capacity reserved for such discontinued DRUG PRODUCT and, provided BSP has the capability to MANUFACTURE such other DRUG PRODUCT(s), BSP

shall MANUFACTURE such other DRUG PRODUCT(s). In such a case, the Parties shall discuss in good faith the terms of the transfer, the equivalence and compensation with respect to the non-absorbed capacity.

4. BSP, upon receipt of a termination notice by UGX, will promptly cease performance of the MANUFACTURING SERVICES or ADDITIONAL SERVICES in progress under the terminated AGREEMENT to the extent applicable, in accordance with a schedule agreed upon by the Parties or unless otherwise advised by UGX and specified in the notice of termination.

2. In addition, UGX shall compensate BSP for:

1. any existing inventories of the applicable DRUG PRODUCT(s) MANUFACTURED by BSP in accordance with the then-current BINDING FORECAST at the MANUFACTURING SERVICE FEE therefor held by BSP as the date of the termination; provided that all terms applicable to the MANUFACTURING and supply of DRUG PRODUCT(s) pursuant to this AGREEMENT and such PRODUCT SCHEDULE shall apply to such DRUG PRODUCT(s), and

2. all PURCHASED MATERIALS acquired by BSP or that BSP is obliged to purchase hereunder and necessary to MANUFACTURE the applicable DRUG PRODUCT(s) is in accordance with BSP's commitment related to the then-current BINDING FORECAST, if applicable, at [***]therefor, [***]%; provided that BSP shall take all reasonable steps to mitigate the costs incurred in connection therewith, and in particular, BSP shall use its best efforts to (A) immediately cancel, to the greatest extent possible, any THIRD PARTY obligations to purchase such PURCHASED MATERIALS and (B) promptly inform UGX of any irrevocable commitments made to purchase such PURCHASED MATERIALS, provided further that the obligations of UGX set forth in this paragraph (b) shall not apply in case this AGREEMENT or any PRODUCT SCHEDULE is terminated by UGX pursuant to Section 20.2.7 (termination for insolvency) or Section 20.2.2 (a) (uncured material).

3. UGX shall arrange for the pick-up from FACILITY of all of FOC MATERIALS and DRUG PRODUCT and supplies owned by UGX within [***] days after the earlier of the termination or expiration of this AGREEMENT. BSP shall charge to UGX a [***] (per [***])] in accordance with Section 9.5. and as set forth in the relevant PRODUCT SCHEDULE.

4. UGX shall be responsible for paying any costs related to [***], in accordance with Section 11.7.

## 7. Miscellaneous.

1. This AGREEMENT constitutes the entire understanding between the Parties as of the EFFECTIVE DATE with respect to the subject matter hereof and supersedes all prior agreements, negotiations, understandings, representations, statements and writings relating thereto.

2. No change of this AGREEMENT and any and all of its Appendixes is valid unless it is in writing and signed by the Parties. This applies also to the foregoing sentence.

3. In case one of the clauses is invalid or unenforceable, the other clauses remain unaffected by this. The Parties shall negotiate in good faith if they wish to replace such invalid or unenforceable clause.

4. Any notice or request required or permitted to be given under or in connection with this AGREEMENT or the subject matter hereof shall be given by prepaid registered or certified first-class airmail, recognized international carrier, e-mail or telefax to the recipient at its address set forth on the first page of this AGREEMENT or to such other address as may have therefore been furnished in writing by the recipient to the sending Party. Any such aforementioned notice or request concerning this AGREEMENT shall be effective upon receipt by the Party to which it is addressed.

5. Neither Party may assign or transfer this AGREEMENT or any rights or obligations hereunder, by operation or law or otherwise, without the prior written consent of the other Party, except that a Party may make such an assignment or transfer, by operation of law or otherwise, without the other Party's consent to its AFFILIATE(S) or to an entity that acquires all or substantially all the business of such Party to which this AGREEMENT relates, whether in a merger, consolidation, reorganization, acquisition, sale or otherwise. Notwithstanding anything to the contrary contained herein,

in the event of an assignment to an AFFILIATE pursuant to this Section 23.5, the assigning Party consents, acknowledges, covenants and guarantees that it shall remain jointly and severally liable, along with the assignee, to the non-assigning Party for all the obligations contained herein. Notwithstanding the foregoing, should any assignee of UGX be a competitor of BSP or has competing business with BSP, BSP shall be [***]. BSP shall not be obligated to permit personnel from such alternative supplier or any of its consultants to enter the FACILITIES. UGX shall be the sole contact with BSP and shall remain jointly liable with such acquirer until the expiration of the shelf life of the last batch manufactured at the Facility. This AGREEMENT shall be binding on the successors and permitted assigns of the assigning Party, and the name of a Party appearing herein shall be deemed to include the name(s) of such Party's successors and permitted assigns to the extent necessary to carry out the intent of this AGREEMENT. Any assignment or attempted assignment by either Party in violation of this Section 23.5, shall be null and void and of no legal effect.

6. Subject to the prior written consent of UGX, BSP may subcontract any part of its performance hereunder. Notwithstanding the foregoing, BSP shall remain responsible and primarily liable for the performance of all BSP's obligations under this Agreement and any breach thereof by any subcontractor within the limitation of liability set forth in Section 16.

7. This AGREEMENT and any potential subsequent amendment to it, if any, and the Product Schedules, maybe executed in 2 (two) or more counterparts, each of which shall be deemed an original and all of which shall constitute together the same instrument. In the event that any signature is delivered by facsimile transmission or by e-mail delivery of a .pdf format data file, such signature shall create a valid and binding obligation of the Party executing (or on whose behalf such signature is executed) with the same force and effect as if such facsimile or ".pdf" signature page were an original thereof.

8. Any controversy, claim or dispute arising out of or relating to this AGREEMENT or the breach thereof shall be settled, if possible, through good-faith negotiation between the Parties. Such good faith negotiations shall commence promptly upon a Party's receipt of notice of any claim or dispute from the other Party and continue for a period [***] CALENDARDAYS. If such efforts are not successful, such controversy, claim or dispute relating to, arising out of, or in any way connected with this AGREEMENT or any term or condition hereof, or the performance by either Party of its obligations hereunder, except as otherwise expressly provided in this AGREEMENT, shall be finally resolved by binding arbitration. Whenever a Party shall decide to institute arbitration proceedings, it shall give written notice to that effect to the other Party. This AGREEMENT shall be governed by and construed in accordance with the Laws of the State of New York without reference to any rules of conflicts of law in force on the date when the notice of arbitration is submitted by either Party and the United Nations Convention on Agreements for the International Sale of Goods is hereby excluded. Disputes shall be resolved through arbitration by an arbitration panel of three (3) arbitrators appointed in accordance with the Rules of the International Chamber of Commerce (the "RULES"). Such arbitration shall take place in New York City, New York, USA and be regulated by the RULES. The arbitral proceedings shall be conducted in English and any award rendered in such arbitral proceedings shall be final and binding upon both Parties. Either Party may enter any arbitration award in any court having jurisdiction or may make an application to any such court for a judicial acceptance of the award and order of enforcement, as the case may be. The Parties' agreement to submit to an arbitration referred to herein shall in no way prevent either Party from exercising its right to terminate this AGREEMENT consistent with the terms set forth in Sections 8 and 20. Either Party may, without inconsistency with this Section, seek from the competent court any provisional remedy that may be necessary to protect their rights or property pending good faith negotiations between the Parties as above described or the establishment of the arbitration.

9. Each Party hereto has a duty of good faith and fair dealing in connection with its performance under this AGREEMENT. Each Party shall perform its obligations under this AGREEMENT in a diligent, legal, ethical and professional manner so as to advance the purposes and intent of this AGREEMENT.

**IN WITNESS WHEREOF,** this Agreement is executed as of the Effective Date on behalf of the parties by their duly authorized representatives.

| | |
|---|---|
| **ULTRAGENYX PHARMACEUTICAL INC.** | **BSP Pharmaceuticals S.p.A.** |
| Dennis Huang | Aldo Braca |
| Chief Technical Operations Officer | President and CEO |

10-Mar-2021

**Exhibit 10.92**

**THIRD AMENDMENT TO LEASE AGREEMENT**

THIS THIRD AMENDMENT TO LEASE AGREEMENT (this "**Third Amendment**") is made as of July 27 , 2022, by and between **ARE-SAN FRANCISCO NO. 17, LLC**, a Delaware limited liability company ("**Landlord**"), and **ULTRAGENYX PHARMACEUTICAL INC.**, a Delaware corporation ("**Tenant**").

**RECITALS**

**A.** Landlord and Tenant are now parties to that certain Lease Agreement dated as of December 15, 2019, as amended by that certain First Amendment to Lease Agreement dated as of September 30, 2020, and as further amended by that certain Second Amendment to Lease Agreement as of October 21, 2020 (as amended, the "**Lease**"). Pursuant to the Lease, Tenant leases certain "**Premises**" consisting of approximately 32,377 rentable square feet of space consisting of (i) approximately 10,781 rentable square feet on the second floor of the Building (the "**Original Premises**"), (ii) approximately 15,116 rentable square feet on the ground floor of the Building (the "**First Expansion Premises**"), and (iii) approximately 6,480 rentable square feet on the ground floor of the Building (the "**Second Expansion Premises**") in that certain building located at 7000 Shoreline Court, South San Francisco, California (the "**Building**"). The Premises are more particularly described in the Lease. Capitalized terms used herein without definition shall have the meanings defined for such terms in the Lease.

**B.** Pursuant to the Work Letter and the First Expansion Premises Work Letter, Landlord agreed to provide TI Allowances to Tenant in the amount of (i) $107,810.00 with respect to the Original Premises, (ii) $513,944.00 with respect to the First Expansion Premises, and (iii) $220,320.00 with respect to the Second Expansion Premises. Tenant has not used the full amount of such TI Allowances.

**C.** Landlord and Tenant desire, subject to the terms and conditions set forth below, to amend the Lease as provided in this Third Amendment.

**NOW, THEREFORE**, in consideration of the foregoing Recitals, which are incorporated herein by this reference, the mutual promises and conditions contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree as follows:

**1.** **Availability of Remaining TI Allowances**. Notwithstanding anything to the contrary contained in the Lease, the Work Letter or the First Expansion Premises Work Letter, Landlord and Tenant agree that (a) any portion of the TI Allowance made available under the Work Letter remaining undisbursed as of the date of this Third Amendment shall remain available, subject to the terms of the Work Letter, through August 31, 2022, and (b) any portion of the TI Allowance made available under the First Expansion Premises Work Letter remaining undisbursed as of the date of this Third Amendment shall remain available, subject to the terms of the First Expansion Premises Work Letter, through August 31, 2022.

**2.** **California Accessibility Disclosure.** The provisions of Section 42(p) of the Lease are hereby incorporated by reference.

**3.** **OFAC**. Tenant and any beneficial owners of Tenant are currently (a) in compliance with and shall at all times during the Term of the Lease remain in compliance with the regulations of the Office of Foreign Assets Control ("**OFAC**") of the U.S. Department of Treasury and any statute, executive order, or regulation relating thereto (collectively, the "**OFAC Rules**"), (b) not listed on, and shall not during the Term of the Lease be listed on, the Specially Designated Nationals and Blocked Persons List maintained by OFAC and/or on any other similar list maintained by OFAC or other governmental authority pursuant to any authorizing statute, executive order, or

regulation, and (c) not a person or entity with whom a U.S. person is prohibited from conducting business under the OFAC Rules.

**4.** **Miscellaneous**.

**a.** This Third Amendment is the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior and contemporaneous oral and written agreements and discussions. This Third Amendment may be amended only by an agreement in writing, signed by the parties hereto.

**b.** This Third Amendment is binding upon and shall inure to the benefit of the parties hereto, their respective successors and assigns.

**c.** This Third Amendment may be executed in 2 or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or any electronic signature process complying with the U.S. federal ESIGN Act of 2000) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes. Electronic signatures shall be deemed original signatures for purposes of this Third Amendment and all matters related thereto, with such electronic signatures having the same legal effect as original signatures.

**d.** Except as amended and/or modified by this Third Amendment, the Lease is hereby ratified and confirmed and all other terms of the Lease shall remain in full force and effect, unaltered and unchanged by this Third Amendment. In the event of any conflict between the provisions of this Third Amendment and the provisions of the Lease, the provisions of this Third Amendment shall prevail. Whether or not specifically amended by this Third Amendment, all of the terms and provisions of the Lease are hereby amended to the extent necessary to give effect to the purpose and intent of this Third Amendment.

**[Signatures on the next page]**

**IN WITNESS WHEREOF**, the parties hereto have executed this Third Amendment as of the day and year first above written.

**LANDLORD:**

**ARE-SAN FRANCISCO NO. 17, LLC**,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership, managing member

By: ARE-QRS CORP.,
a Maryland corporation, its General Partner

By: /s/ William Barrett
Name: William Barrett
Its: Vice President - Real Estate Legal Affairs

**TENANT:**

**ULTRAGENYX PHARMACEUTICAL INC**.,
a Delaware corporation

By: /s/ Emil D. Kakkis, M.D., Ph.D. Name: Emil D. Kakkis, M.D., Ph.D. Its: CEO

□X I hereby certify that the signature, name, and title above are my signature, name and title

**Exhibit 10.95**

LEASE

BY AND BETWEEN

BRICKBOTTOM I QOZB LP
LANDLORD

AND

ULTRAGENYX PHARMACEUTICAL INC. TENANT

100 Chestnut Street
Somerville, Massachusetts

**NOTE: See Subsection 6.1.9 for provision regarding Tenant's request for Landlord's consent to Alterations and removal of the Alterations.**

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LEASE

100 Chestnut Street
Somerville, Massachusetts

Article 1
Reference Data

1.1 Introduction and Subjects Referred To.

This is a lease (this "Lease") entered into by and between BRICKBOTTOM I QOZB LP, a Delaware limited partnership transacting business in Massachusetts as BRICKBOTTOM I QOZB LIMITED PARTNERSHIP ("Landlord") and ULTRAGENYX PHARMACEUTICAL INC., a Delaware corporation ("Tenant").

Each reference in this Lease to any of the following terms or phrases shall be construed to incorporate the corresponding definition stated in this Section 1.1.

Date of this Lease: August 18, 2022.

Building and Property: That four-story office and laboratory building to be constructed by Landlord (the "Building") on the parcel of land in the City of Somerville, Massachusetts known as and located at 100 Chestnut Street (the "Land") as shown on Exhibit A-1 attached hereto. The Building and the land parcels on which it is located and the sidewalks adjacent thereto are hereinafter collectively referred to as the "Property "Property".

Premises: A portion of the second (2nd) floor of the Building, substantially as shown on Exhibit A-1 hereto.

Premises Rentable Area: 42,580 rentable square feet as shown on Exhibit A-2 attached hereto, subject to Section 2.3 below, which may be configured to achieve a 65-35 lab to office ratio on the first 36,437 rentable square feet of Premises Rentable Area and a 60-40 lab to office ratio on the remaining square feet of Premises Rentable Area.

Building Rentable Area: 208,616 square feet.

Original Term: Six (6) years and four (4) months, beginning on the Commencement Date and expiring on the day preceding the sixth

Rent Commencement

(6th) anniversary of the Rent Commencement Date, except that if the Rent Commencement Date shall occur on a day other than the first day of a month, the Original Term shall expire on the last day of the month in which such anniversary shall occur.

Date: The date that is four (4) months after the Commencement Date.

Lease Year: Each consecutive twelve (12) calendar month period immediately following the preceding Lease Year, beginning on the Commencement Date, except that Lease Year 1 shall also include the period from the Commencement Date through the day before the Rent Commencement Date and the succeeding twelve (12) month period beginning on the Rent Commencement Date, and, if the Rent Commencement Date does not occur on the first day of a calendar month, Lease Year 1 shall also include the partial calendar month during which the first anniversary of the Rent Commencement Date occurs; with each succeeding Lease Year being the period of twelve (12) consecutive calendar months following the preceding Lease Year

Annual Fixed Rent: The following amounts, subject to adjustment as set forth in Section 3.6:

| Months | Annual Fixed Rent PRSF per annum | Annual Fixed Rent | Monthly Installments |
|---|---|---|---|
| 1-4 (Lease Year 1) | $0.00 | $0 | $0 |
| 5-16 (Lease Year 1) | $123.92 | $5,276,513.60 | $439,709.47 |
| 17-28 (Lease Year 2) | $126.47 | $5,385,092.60 | $448,757.72 |
| 29-40 (Lease Year 3) | $129.10 | $5,496,928.97 | $458,077.41 |
| 41-52 (Lease Year 4) | $131.80 | $5,612,120.43 | $467,676.70 |
| 53-64 (Lease Year 5) | $134.59 | $5,730,767.64 | $477,563.97 |
| 65-76 (Lease Year 6) | $137.46 | $5,852,974.26 | $487,747.85 |

* Tenant shall not be obligated to pay Annual Fixed Rent for the four (4) month period beginning on the Commencement Date and ending on the day before the Rent Commencement Date. If the

Rent Commencement Date is other than the first day of a calendar month, Tenant shall pay Annual Fixed Rent for the month in which the first anniversary of the Rent Commencement Date occurs in an amount which is equal to $439,709.47 multiplied by a fraction, the numerator of which is the number of days from the first anniversary of the Rent Commencement Date through the last day of the month in which the first anniversary of the Rent Commencement Date occurs (inclusive of both dates) and the denominator of which is the number of days in such full calendar month.

Annual Fixed Rent as set forth in the schedule above is comprised of the Base Rent and the Financed-Fit-Out Rent, as follows:

"Base Rent" shall mean

| Months | Base Rent PRSF per Annum | Annual Base Rent | Monthly Base Rent |
|---|---|---|---|
| 1-4 (Lease Year 1) | $0 | $0 | $0 |
| 5-16 (Lease Year 1) | $85.00 | $3,619,300.00 | $301,608.33 |
| 17-28 (Lease Year 2) | $87.55 | $3,727,879.00 | $310,656.58 |
| 29-40 (Lease Year 3) | $90.18 | $3,839,715.37 | $319,976.28 |
| 41-52 (Lease Year 4) | $92.88 | $3,954,906.83 | $329,575.57 |
| 53-64 (Lease Year 5) | $95.67 | $4,073,554.04 | $339,462.84 |
| 65-76 (Lease Year 6) | $98.54 | $4,195,760.66 | $349,646.72 |

"Financed Fit-Out Rent" shall mean**:

| Months | Financed Fit-Out Rent PRSF per Annum | Annual Financed Fit-Out Rent | Monthly Financed Fit-Out Rent |
|---|---|---|---|
| 1-4 (Lease Year 1) | $0 | $0 | $0 |

| | | | |
|---|---|---|---|
| 5-16 (Lease Year 1) | $38.92 | $1,657,213.60 | $138,101.13 |
| 17-28 (Lease Year 2) | $38.92 | $1,657,213.60 | $138,101.13 |
| 29-40 (Lease Year 3) | $38.92 | $1,657,213.60 | $138,101.13 |
| 41-52 (Lease Year 4) | $38.92 | $1,657,213.60 | $138,101.13 |
| 53-64 (Lease Year 5) | $38.92 | $1,657,213.60 | $138,101.13 |
| 65-76 (Lease Year 6) | $38.92 | $1,657,213.60 | $138,101.13 |

** Subject to prepayment as provided in Section 4.1.

Tenant's Percentage: The fraction, expressed as a percentage, the numerator of which is the Rentable Floor Area of Premises and the denominator of which is the Rentable Floor Area of Building, which is twenty and forty- one hundredths percent (20.41%), subject to adjustment as provided in Section 2.6.

Permitted Uses: General administrative and sales office purposes, life science discovery and development, preclinical research, clinical research, QC testing, pilot plant operations, and other manufacturing support functions, engineering, laboratory, partnership/special purpose vehicle/university/hospital collaboration, sales and marketing, employee training, storage and/or warehouse and other lawful ancillary uses that are (i) consistent with first class life science/R&D/office facilities in the Greater Boston Area, (ii) in compliance with all applicable laws, and (iii) not conducted by a government, local state or federal agency, in all events subject to the provisions of Subsection 6.1.2.

Delivery Date: September 1, 2023.

Security Deposit: Equal to six (6) months of the Annual Base Rent due per month for Months 5-16 in the schedule above (initially, $1,809,650.00) subject to adjustment as set forth in Section 3.6 and to reduction as set forth in Section 4.7.

Commercial General Liability Insurance Limits: $5,000,000 per occurrence.

Original Address of Landlord: BRICKBOTTOM I QOZB LP
NRL Manager

c/o North River
Company 610 West 26th
Street
New York, NY 10001
Attn: Christopher S.
Flagg

Landlord's Agent: NRL Manager or such other entity as shall be designated by Landlord from time to time.

Original Address of
Tenant: Ultragenyx Pharmaceutical Inc.
Legal
Department
60 Leveroni
Court
Novato, CA 94949

Account for Payment
of Rent: Bank Name: First Republic Routing No.:
321081669
Account Name: BRICKBOTTOM I QOZB LP (DACA)
Account No.: 80010662806

1.2 Exhibits.

The Exhibits listed below in this section are incorporated in this Lease by reference and are to be construed as a part of this Lease.

EXHIBIT A-1. Plan of Land with Building Footprint EXHIBIT
A-2. Plan showing the Premises.
EXHIBIT A-3. Landlord's Work.
EXHIBIT A-4. Work Matrix.
EXHIBIT A-5. Laboratory and Office Basis of Design. EXHIBIT
A-6. Preliminary Pricing.
EXHIBIT A-7. Preliminary Long Lead Items.
EXHIBIT B. Rules and Regulations.
EXHIBIT C. Alterations Requirements.
EXHIBIT D. Contractor's Insurance Requirements.
EXHIBIT E. Intentionally Omitted.
EXHIBIT F. Declaration By Landlord and Tenant. EXHIBIT G.
Tenant Design and Construction Guidelines. EXHIBIT H. Mobility
Management Plan.
EXHIBIT I. Form of Shared Space Arrangement. EXHIBIT
J. Form of Non-Disturbance Agreement. EXHIBIT K. Form
of Letter of Credit.
EXHIBIT L. Waste Storage Location.
EXHIBIT M. Financed Fit-Out Rent Amortization Schedule.

Article 2

Premises and Term

2.1 Premises. Landlord hereby leases the Premises to Tenant and Tenant hereby leases the Premises from Landlord, subject to and with the benefit of the terms, covenants, conditions and provisions of this Lease, excluding exterior faces of exterior walls, the common lobbies, hallways, stairways, stairwells, elevator shafts and other common areas, and the escalators, elevators, pipes, ducts, conduits, wires and appurtenant fixtures and other common facilities serving the common areas, the Premises and the premises of other tenants in the Building.

Tenant shall have, as appurtenant to the Premises, rights to use, in common with others, subject to the Rules and Regulations (as defined in Subsection 6.1.9) : (a) the common lobbies, hallways and stairways of the Building, (b) the common elevators, loading docks, pipes, ducts, conduits, wires and appurtenant fixtures and other common facilities serving the Premises, (c) common walkways and driveways (if any) necessary for access to the Building, (d) if the Premises include less than all of the rentable area of any floor of the Building, the common toilets and other common facilities located on such floor, and (e) the Laboratory Systems. "Laboratory Systems" shall mean all base Building systems, fixtures and equipment provided by Landlord from time to time for the use in common by tenants and occupants of the Building which support laboratory uses in the Building. As of the Commencement Date, the Laboratory Systems shall include the following: pH neutralization systems, chemical storage room and a waste accumulation room. Landlord shall not (i) reduce the number of parking spaces available for use of tenants of the Building except to the extent required by law or the MMP, as defined in Subsection 6.1.2, (ii) alter the common areas and the common facilities in such a manner as would materially adversely affect Tenant's access to the Premises, (iii) alter the common facilities and common areas, including but not limited to the Laboratory Systems, which would cause Tenant to incur expenses (other than de minimis amounts) or which would, to more than a de minimis extent, adversely alter, reduce or remove any component of the common facilities including, but not limited to, the Laboratory Systems, which exist as of the Commencement Date or which is thereafter included within the Laboratory Systems, or (iv) enter into a declaration of covenants or reciprocal easement agreement or otherwise restrict or bind the Property or Building which would cause Tenant to incur additional expenses or which would reduce
Tenant's rights or increase Tenant's obligations under this Lease other to a de minimis degree.

2.2 Term. The term of this Lease shall be for a period beginning on the Commencement Date (as defined in Section 3.1) and continuing for the Original Term and any extension of the term hereof in accordance with the provision of this Lease, unless sooner terminated as hereinafter provided. When the dates of the beginning and end of the Original Term have been determined such dates shall be evidenced by a confirmatory document executed by Landlord and Tenant in the form substantially as shown on Exhibit F hereto and delivered each to the other, but the failure of Landlord and Tenant to execute or deliver such document shall have no effect upon such dates. The Original Term and any extension of the term hereof in accordance with the provisions of this Lease is hereinafter referred to as the "term" of this Lease.

2.3 Expansion Option. Tenant shall have the ongoing option, continuing until the date which is nine (9) months prior to the estimated Rent Commencement Date (i.e., March 31, 2023) (the "Expansion Option End Date"), to elect to lease all or any portion of the remaining 18,353 rentable square feet of space located on the second (2nd) floor of the Building (the "Expansion Area") on the same terms and conditions as the initial Premises by delivering not more than two (2) notices to Landlord (each, an "Expansion Option Notice") at any time following the Date of this Lease, but not later than the Expansion Option End Date, time being of the essence. If Tenant elects to lease less than all of the Expansion Area in its first Expansion Option Notice, Tenant shall have the ongoing right to elect all or any portion of remaining Expansion Area until the Expansion Option End Date; provided, however, that if Tenant shall elect to lease less than all of the Expansion Area it may not elect to lease more than 12,353 rentable square feet of the Expansion Area (such that there shall remain at least 6,000 rentable square feet of space on the second (2nd) floor of the Building if Tenant elects to lease less than all of the Expansion Area). If Tenant elects to lease all of the Expansion Area, the Premises Rentable Area (i.e. the aggregate square footage of the Premises and the Expansion Area) shall be 60,933 rentable square feet. Tenant shall specify in its Expansion Option Notice the square footage and approximate location of the portion of the Expansion Area which Tenant has elected to lease. If an Expansion Option Notice is for less than all of the Expansion Area, Landlord and Tenant shall work together in good faith to mutually agree upon a reasonable configuration and layout of the premises Tenant has elected to lease, plus or minus such additional space as may be reasonably required so that such space and any remaining space on the second (2nd) floor of the Building (which in no event shall be less than 6,000 rentable square feet) are both situated and configured so as to be reasonably marketable and so that the space Tenant has elected to lease is contiguous with the Premises, as may be expanded, and a construction and delivery schedule for such Expansion Area. In no event shall Landlord's obligation for any penalties related to the Existing Lease, as defined in Section 3.1 below, apply to the delivery of any of the Expansion Space. The parties shall execute an amendment to this Lease within thirty (30) days following an Expansion Option Notice, in a commercially reasonable form prepared by Landlord and reasonably acceptable to Tenant, memorializing the expansion of the Premises, amending the terms of this Lease which vary with the Premises Rentable Area (including but not limited to, the Annual Fixed Rent, Tenant's Percentage, the Allowance, and the number of Parking Spaces allocated to Tenant), confirming that the lease of such Expansion Area shall be on the same terms and conditions as this Lease, and confirming that all terms, covenants, conditions, and provisions of the Lease remain unmodified with the exception of those items which would be affected by the expansion, as the case may be. The Parties hereby agree that the Annual Fixed Rent for the Expansion Area shall include the Financed Fit-Out Rent only to the extent that Landlord provides the same financing for tenant improvements in the Expansion Area which is the basis of the Financed Fit-Out Rent. Landlord shall not lease any of the Expansion Area to a third party unless Tenant fails to exercise its rights prior to the Expansion Option End Date to lease such Expansion Area. If Landlord enters into a letter of intent to lease, a license or other occupancy agreement for all or any portion of the Expansion Area prior to the Expansion Option End Date, Landlord shall explicitly provide that such letter of intent, license or occupancy agreement is subject to and subordinate to Tenant's rights hereunder to lease the Expansion Area.

2.4 Extension Option. So long as this Lease is still in full force and effect, and subject to the Conditions (as hereinafter defined), which Landlord may waive, in its discretion, at

any time, but only by notice to Tenant, Tenant shall have the right to extend the term of this Lease for two (2) additional periods (the "Extended Term(s)") of five (5) years each, commencing on the day succeeding the expiration of the Original Term or the preceding Extended Term, as the case may be, and ending on the day immediately preceding the fifth (5th) anniversary of the commencement of such Extended Term. All of the terms, covenants and provisions of this Lease applicable immediately prior to the expiration of the then current term (i.e. Original Term or Extended Term, as applicable) shall apply to each Extended Term except that (i) the Annual Fixed Rent for each Extended Term shall be the Market Rate (as hereinafter defined) for the Premises determined as of the date of the Election Notice, as designated by
Landlord by notice to Tenant ("Landlord's Notice"), but subject to Tenant's right to dispute as hereinafter provided; and (ii) Tenant shall have no further right to extend the term of this Lease beyond the Extended Terms hereinabove provided. If Tenant shall elect to exercise any of the aforesaid options, it shall do so by giving Landlord notice (an "Election Notice") of its election not later than twenty-four (24) months, nor sooner than twelve (12) months, prior to the expiration of the then current term of this Lease (Original Term or Extended Term, as applicable). If Tenant fails to give any such Election Notice to Landlord or the Conditions are neither satisfied nor waived by Landlord, the term of this Lease shall automatically terminate no later than the end of the term then in effect, and Tenant shall have no further option to extend the term of this Lease, it being agreed that time is of the essence with respect to the giving of any such Election Notice. If Tenant shall extend the term hereof pursuant to the provisions of this Section 2.4, such extension shall (subject to satisfaction of the Conditions, unless waived by Landlord) be automatically effected without the execution of any additional documents, but
Tenant shall, at Landlord's request, execute an agreement confirming the Annual Fixed Rent for the applicable Extended Term. The "Conditions" are that, as of the date of the applicable Election Notice there shall exist no Default of Tenant and Tenant, its assignees and/or subtenants shall actually occupy, in the aggregate, at least eighty percent (80%) of the entire Premises.

"Market Rate" shall mean the then fair market annual rent (determined as set forth below), at the time of the Election Notice, for premises in the greater Somerville market (the "Market") comparable to the Premises in terms of location within a building, finish, age, building quality and amenities, under terms and conditions substantially the same as those of this Lease, in "as-is" condition taking into account the condition of the Premises and the improvements and finishes therein, for those portions of the Premises which are built-out for research and development laboratory uses, to the extent such improvements and finishes would be generally provided in premises devoted to research and development laboratory uses (but not taking into consideration any improvements and finishes in the Premises that are customized or were installed specifically for the use of Ultragenyx Pharmaceuticals Inc.) for comparable periods of time, and taking into account all relevant factors such as free rent periods, tenant improvement allowances then being offered in the Market and the effect of same on base rent (by means of example only, if the Market Rate for a five (5) year renewal term is determined to be $100.00 per rentable square foot per annum, but it is determined that such Market Rate contemplates a tenant improvement allowance in the amount of $25.00 per rentable square foot and Tenant elects not to receive a tenant improvement allowance in connection with the Extended Term, the Market Rate shall be reduced by $6.08 per rentable square foot per annum assuming an eight percent (8%) amortization of the tenant improvement allowance Tenant elects not to receive), the manner, if any, in which Landlord is reimbursed for taxes and operating expenses, and brokerage commissions; but which Market Rate shall be determined without

regard to the Annual Fixed Rent in effect immediately prior to the commencement of the Extended Term, the parties acknowledging that the Annual Fixed Rent for the Original Term was determined based, in part, on the cost of improvements to the Premises. At any time during the last two (2) years of any applicable term, within thirty (30) days following a request of Tenant,
Landlord shall provide Tenant with Landlord's designation of the Annual Fixed Rent for the coming potential Extended Term. If Tenant disagrees with Landlord's designation of the Market Rate, then Tenant shall give notice thereof to Landlord within twenty (20) days after Landlord's Notice (failure to provide such notice of disagreement within such 20-day period constituting acceptance by Tenant of Market Rate as set forth in Landlord's Notice); and if the parties cannot agree upon the Market Rate by the date that is thirty (30) days following Landlord's Notice, then the Market Rate shall be submitted to appraisal as follows: Within fifteen (15) days after the expiration of such thirty (30) day period, Landlord and Tenant shall each give notice to the other specifying the name and address of the appraiser each has chosen. The two appraisers so chosen shall meet within ten (10) days after the second appraiser is appointed and if, within twenty (20) days after the second appraiser is appointed, the two appraisers shall not agree upon a determination of the Market Rate in accordance with the following provisions of this Section 2.4 they shall together appoint a third appraiser. If only one appraiser shall be chosen whose name and address shall have been given to the other party within such fifteen (15) day period and who shall have the qualifications hereinafter set forth, that sole appraiser shall render the decision which would otherwise have been made as hereinabove provided. All appraisers referenced in this Section 2.4 shall be informed that they must act in a commercially reasonable manner and in good faith.

If said two appraisers cannot agree upon the appointment of a third appraiser within ten (10) days after the expiration of such twenty (20) day period, then either party, on behalf of both and on notice to the other, may request such appointment by the then President of the Greater Boston Real Estate Board (or any similar or successor organization) for the greater Somerville, Massachusetts area in accordance with its then prevailing rules. If said President shall fail to appoint said third appraiser within ten (10) days after such request is made, then either party, on behalf of both and on notice to the other, may request such appointment by the American Arbitration Association (or any successor organization) in accordance with its then prevailing rules. In the event that all three appraisers cannot agree upon such Market Rate within ten (10) days after the third appraiser shall have been selected, then each appraiser shall submit his or her designation of such Market Rate to the other two appraisers in writing; and Market Rate shall be determined by calculating the average of the two numerically closest (or, if the values are equidistant, all three) values so determined.

Each of the appraisers selected as herein provided shall have at least ten (10) years' experience as a commercial real estate broker in the greater Somerville area dealing with properties of the same type and quality as the Building. Each party shall pay the fees and expenses of the appraiser it has selected and the fees of its own counsel. Each party shall pay one half (1/2) of the fees and expenses of the third appraiser (or the sole appraiser, if applicable) and all other expenses of the appraisal. The decision and award of the appraiser(s) shall be in writing and shall be final and conclusive on all parties, and counterpart copies thereof shall be delivered to both Landlord and Tenant. Judgment upon the award of the appraiser(s) may be entered in any court of competent jurisdiction.

The appraiser(s) shall determine the Market Rate of the Premises for the applicable Extended Term and render a decision and award as to their determination to both Landlord and Tenant (a) within twenty (20) days after the appointment of the second appraiser, (b) within twenty (20) days after the appointment of the third appraiser or (c) within fifteen (15) days after the appointment of the sole appraiser, as the case may be. In rendering such decision and award, the appraiser(s) shall assume (i) that neither Landlord nor the prospective tenant is under a compulsion to rent, and that Landlord and Tenant are typically motivated, well-informed and well-advised, and each is acting in what it considers its own best interest, (ii) the Premises are fit for immediate occupancy and use "as is" (taking into account the factors set forth above in this Section 2.4 for the determination of Market Rate), (iii) that in the event the Premises have been damaged by fire or other casualty prior to the commencement of the applicable Extended Term, they have been fully restored. The appraisers shall also take into consideration the rents contained in leases for comparable space in the Building, or in comparable buildings in the greater Somerville area, for comparable periods of time.

If the dispute between the parties as to the Market Rate has not been resolved before the commencement of Tenant's obligation to pay the Annual Fixed Rent based upon determination of such Market Rate, then Tenant shall pay the Annual Fixed Rent under the Lease based upon the Market Rate designated by Landlord in Landlord's Notice until either the agreement of the parties as to the Market Rate, or the decision of the appraiser(s), as the case may be, at which time Tenant shall pay any underpayment of the Annual Fixed Rent to Landlord, or Landlord shall refund any overpayment of the Annual Fixed Rent to Tenant.

Landlord and Tenant hereby waive the right to an evidentiary hearing before the appraiser(s) and agree that the appraisal shall not be an arbitration nor be subject to state or federal law relating to arbitrations.

2.5 Measurement of the Premises. Either party hereto may, not later than ten (10) days after the Commencement Date, request that an exact measurement of the Premises be made in accordance with the Standard Method of Measuring Floor Area in Office Buildings as adopted by the Building Owners and Managers Association International (ANSI/BOMA Z65.1-2017). Such measurement shall be made by a licensed architect or engineer designated by Landlord at the cost and expense of the requesting party.

If the rentable area of the Premises, as so measured, is more than one hundred one percent (101%) or less than ninety-nine percent (99%) of the Premises Rentable Area as set forth in Section 1.1: (i) the definition of Premises Rentable Area set forth in Section 1.1 shall be deemed amended in accordance with such measurement; (ii) Annual Fixed Rent shall, retroactively to the Commencement Date, be recomputed by multiplying the Annual Fixed Rent as set forth in Section 1.1 by a fraction (the "Fraction"), the numerator of which shall be the rentable area as so measured and the denominator of which shall be the Premises Rentable Area set forth in Section 1.1; (iii) Tenant's Percentage shall, retroactively to the Commencement Date, be recomputed to be the percentage determined by multiplying Tenant's Percentage as set forth in Section 1.1 by the Fraction, and (iv) if applicable, the Allowance shall, retroactively to the Commencement Date, be adjusted by multiplying the rentable area as so measured by the Allowance per rentable square foot as set forth in Article 3 below.

Any payment due to Landlord as the result of such adjustment shall be paid within thirty (30) days after notice to Tenant of such computation. Any payment due to Tenant as a result of such adjustment shall be credited against installments of Annual Fixed Rent thereafter becoming due.

In the event of any adjustment pursuant to this Section 2.5, Landlord and Tenant shall promptly execute a written statement setting forth the recomputed Premise Rentable Area, Annual Fixed Rent, Tenant's Percentage and (if applicable) the Allowance, but the failure by either party to execute such a statement shall have no effect on the validity of such recomputation.

If (i) neither Landlord nor Tenant requests any adjustment as herein provided within the time limit provided, or (ii) such adjustment is requested, but the rentable area is within the two (2%) percent range set forth above, Annual Fixed Rent, Tenant's Percentage, and Premises Rentable Area shall remain as set forth in Section 1.1, and neither Landlord nor Tenant shall have any right to any adjustment and shall not be subject to remeasurement.

## Article 3
## Commencement and Condition

3.1 Commencement Date. The Commencement Date shall be the date on which Landlord delivers the Premises to Tenant with Landlord's Work and Tenant's Work Substantially Complete, as such terms are hereinafter defined. Landlord shall use diligent efforts to cause the Commencement Date to occur prior to the Delivery Date; provided, however, that the Commencement Date shall be no earlier than July 1, 2023. If the Commencement Date has not occurred by the Delivery Date for reasons other than Force Majeure or Tenant Delay (as such terms are hereinafter defined), then for each of the first thirty (30) days of any such failure Tenant shall be entitled to a one (1) day delay in the Rent Commencement Date and for each subsequent day of any such failure Tenant shall be entitled to a two (2) day delay of the Rent Commencement Date; and if Landlord shall fail to deliver the Premises to Tenant by February 28, 2024 (i.e., 180 days after the Delivery Date) for reasons other than Force Majeure or Tenant Delay then, in addition to the delays in the Rent Commencement Date described above, Tenant shall have the right to terminate this Lease by giving notice to Landlord not later than sixty (60) days after the expiration of such one hundred eighty (180) day period; and this Lease shall cease and come to an end without further liability or obligation on the part of either party ten (10) days after the giving of such notice, it being agreed that time is of the essence with respect to the giving of such notice.

In addition, if Landlord shall fail to deliver the Premises to Tenant by the Delivery Date with Landlord's Work and Tenant's Work Substantially Complete ("Landlord's Late Delivery") for reasons other than Force Majeure or Tenant Delay, Landlord shall (a) reimburse Tenant for all amounts paid by Tenant as holdover rent over and above the sum of base or fixed rent plus additional rent that was due immediately prior to any such holdover over ("Hold Over Rent") under Tenant's existing lease (the "Existing Lease") at 840 Memorial Drive, Cambridge, Massachusetts; such payments shall be made to Tenant within thirty (30) days following request for reimbursement therefore, given together with reasonable supporting documentation, and (b)

Landlord shall indemnify, defend, protect, and hold harmless Tenant and the Tenant Parties from and against any and all loss, cost, damage, expense and liability (including, without limitation, court costs and reasonable attorneys' fees) incurred in connection with or arising from such holdover under the Existing Lease and save and hold other tenants, agents, employees, patients, visitors, invitees or licensees harmless against any damages, liability, claims, causes of action or judgments arising therefrom; provided, however, that Landlord's reimbursement obligations under this clause (b) shall not exceed $1,800,000.00. Landlord hereby acknowledges that the Hold Over Rent due under the Existing Lease is due on a monthly basis and, accordingly, if there is a Landlord's Late Delivery of the Premises the Hold Over Rent will not be prorated for a partial month, but shall be due for one or more months in their entirety. Upon receipt of notice from Landlord notifying Tenant of Landlord's Late Delivery, Tenant shall use reasonable efforts, at Landlord's sole cost and expense, to mitigate its damages under its Existing Lease including, without limitation, using commercially reasonable efforts to extend the term of the Existing Lease in order to avoid being liable for Hold Over Rent and/or requesting that the Hold Over Rent due under the Existing Lease be prorated on a daily basis, and Landlord shall pay (i) the out-of-pocket cost of such efforts made by Tenant and (ii) all payments, rent and additional rent for and during such extension term of the Existing Lease as set forth in this Section 3.1. Tenant hereby represents that current termination date of the Existing Lease is December 31, 2023 and, unless the Commencement Date occurs on or before December 31, 2023, Tenant shall not agree to an earlier expiration or termination of the term of the Existing Lease. Tenant's right to a postponement of the Rent Commencement Date, reimbursement of its holdover penalties and
Tenant's termination right pursuant to this Section 3.1 shall be Tenant's sole and exclusive remedy at law or in equity for Landlord's failure to Substantially Complete Landlord's Work and Tenant's Work and deliver the Premises to Tenant as required herein.

3.2 Landlord's Work. Landlord is in the process of constructing the Building at the Property. Landlord, at Landlord's sole cost and expense shall construct Landlord's initial construction of the Building including, but not limited to, all shell and core improvements for the Building (including the underground parking garage), all landscaping, plaza areas, walkways, driveways, sidewalks, Building amenities and other improvements on the Land, and shall construct the Building and the Premises and perform certain base building improvements to prepare the Premises for Tenant's Work (as defined below), as such construction and improvements are shown on Exhibit A-3 attached hereto, including those items listed under "LL" on the Landlord/Tenant Work Matrix (the "Work Matrix") attached hereto as Exhibit A-4 (collectively, "Landlord's Work"). Landlord's Work and Tenant's Work shall be constructed by Consigli Construction (or a licensed and qualified contractor with substantial experience in constructing life sciences office and laboratory space reasonably selected by Landlord if Landlord reasonably determines that Consigli Construction will not be able to complete Landlord's Work and Tenant's Work) ("Landlord's Contractor"). Landlord shall cause Landlord's Contractor to construct Landlord's Work and Tenant's Work in a good and
workmanlike manner, in accordance with applicable laws and building codes, in compliance with applicable permits for Landlord's Work and Tenant's Work, and in accordance with Landlord's Plans and Tenant's Plans. Landlord shall deliver possession of the Premises to Tenant and Tenant agrees to accept the Premises with Landlord's Work and Tenant's Work Substantially Complete. Tenant acknowledges that except as set forth in this Section 3.2, it is not relying on any representations of Landlord or Landlord's agents or employees as to the current condition or

the condition of Landlord's Work or Tenant's Work, and Landlord shall have no obligation with respect thereto except as may be expressly set forth in this Lease.

The materials and equipment furnished in the performance of Landlord's Work and Tenant's Work will be of good quality (consistent with first-class office and laboratory spaces, as the case may be), new and of recent manufacture and Landlord's Work and Tenant's Work, all components thereof and the Building Systems shall be in good working order and condition as of the completion of Landlord's Work. On the Commencement Date the Building including, but not limited to, the roof and foundation will be in good condition and leak-free. If it is determined that the roof or foundation is not in such condition as of the Commencement Date, Landlord shall cause the same to be put in such condition promptly after having notice thereof, and all costs and expenses of such corrective work shall be excluded from Operating Costs.

3.3 Tenant's Work.

(a) Tenant shall, not later than August 26, 2022 (the "Design Submission Date"), submit to Landlord for Landlord's approval as set forth herein a set of design development plans ("Interim Plans") for the initial improvements to the Premises desired by Tenant, which Interim Plans shall be consistent with the Work Matrix and with the laboratory and office basis of design titled Laboratory Basis of Design dated June 03, 2021, and updated as of June 03, 2022, the cover page of which is attached hereto as Exhibit A-5 and the full document of which can be found at: <https://www.dropbox.com/s/90b0cqq4kmcgndh/ULTRAGENYX%20%20BOD%20D RAFT%202022.06.03.pdf?dl=0>

Landlord hereby approves the Laboratory Basis of Design (the "BOD," and, together with the Work Matrix, hereinafter referred to as the "Schematic Plans"). Both Landlord and Tenant acknowledge and agree that the entire Laboratory Basis of Design is not attached to this Lease due to its large size, but the 146 page document was provided to Landlord by Tenant prior to the Date of this Lease and it is expressly incorporated herein as Exhibit A-5. In the event of a conflict between the Work Matrix and the BOD as to whether any of the initial improvements to the Premises belong in the Landlord, Tenant, or Work by Tenant column, the Work Matrix shall control; in the event of a conflict between the Work Matrix and the BOD as to the specificity of any item of the initial improvements to the Premises, the BOD shall control; provided, however, that notwithstanding anything in the Work Matrix or the BOD to the contrary, Landlord shall provide three (3) fume hoods as part of Tenant's Work. Not later than October 7, 2022 (the "Plan Submission Date"), Tenant shall submit to Landlord for Landlord's approval as set forth herein a full set of construction drawings and specifications ("Tenant's Plans") for the initial improvements to the Premises desired by Tenant (collectively with the Interim Plans and the Schematic Plans, the "TI Plans"), which Tenant's Plans shall, within five (5) days following approval thereof by Landlord, be submitted by Landlord or its contractor to the City of Somerville together with an application for a building permit for Tenant's Work. The TI Plans shall be prepared by Jacobs Wyper Architects, which Landlord hereby approves as Tenant's architect. Tenant's Plans shall consist of a full set of detailed, coordinated construction plans and specifications for the work necessary to perform Tenant's Work (as defined below) and in suitable form for filing an application for a building permit with the City of Somerville.
Landlord shall respond to the initial submissions of the Interim Plans and Tenant's Plans (either

by approval, request for additional information, request for revision or communication of a reasonably detailed reason for failure to approve) within ten (10) Business Days after the date of Landlord's receipt thereof and to any re-submission within five (5) Business Days after receipt thereof ("Landlord's Review Period"), and Landlord's approval shall not be unreasonably withheld, conditioned or delayed, provided that notwithstanding the foregoing, Landlord's determination of matters relating to aesthetic issues relating to alterations or changes visible outside the Premises shall be in Landlord's sole discretion. Landlord's approval is solely given for the benefit of Landlord under this Lease and neither Tenant nor any third party shall have the right to rely upon Landlord's approval of the TI Plans for any other purpose whatsoever.
Without limiting the foregoing, Tenant shall be responsible for all elements of the design of the TI Plans for the Premises (including, without limitation, compliance with all applicable laws, codes and regulations, functionality of design, the structural integrity of the design, the configuration of the Premises and the placement of Tenant's furniture, appliances and equipment), and Landlord's approval of the TI Plans shall in no event relieve Tenant of the responsibility for such design; provided however, Landlord shall be responsible for all elements of design of the Common Areas of the Building outside of the Premises and compliance with all applicable laws, codes and regulations and functionality of design, the structural integrity of the design, the configuration of the Building and the Common Areas. In addition, Landlord shall have the right to withhold approval of any alterations or work shown on the TI Plans to the extent that such alterations or work are inconsistent with the Schematic Plan or the Work Matrix (provided that such approval shall not be unreasonably withheld, conditioned or delayed), that materially increases the scope of Landlord's Work or Tenant's Work or that materially increases the cost thereof beyond what is contemplated by the Schematic Plan and the Work Matrix, unless Tenant agrees, in Tenant's sole discretion, agrees to pay for such material increase in cost.

(b) The parties acknowledge that it is in their mutual interest to ensure that the Commencement Date occurs not later than the Delivery Date and that the Total TI Costs do not exceed the Maximum Turnkey Amount, as such terms are defined below. To that end, Landlord shall share Landlord's proposed construction schedule with Tenant, and any revisions thereto, on a regular basis and, in connection with its review of Tenant's Plans, Landlord shall provide a commercially reasonable final construction schedule and budget. In addition, at the time of review of the Interim Plans and the Tenant's Plans, Landlord shall identify and notify Tenant of any items contained therein, which were not contained in or contemplated by the Schematic Plans or the Work Matrix, that Landlord's Contractor identified as "Long Lead Items" (items for which there is a long lead time in obtaining the materials therefor or which are specially or specifically manufactured, produced or milled for the work in or to the Premises and require additional time for receipt or installation such that Landlord's Contractor reasonably determines will cause Landlord's Work and/or Tenant's Work not to be Substantially Complete by the Delivery Date and which were not contained in or contemplated by the Schematic Plans or the Work Matrix, Landlord having already identified Long Lead Items contained in the Work Matrix and Schematic Plans (as such items are shown on Exhibit A-7 attached hereto); provided, however, Landlord acknowledges and agrees that it is Landlord's obligation to deliver, and the scope of Tenant's Work is intended to include, those systems, equipment and improvements customarily included in first class commercial laboratory and office space, which may include items for which there are long lead times, and in no event shall such items be deemed to be Long Lead Items to which Landlord may object except to the extent that Tenant's Plans contain requirements not contemplated by the Schematic Plans or the Work Matrix and for which Tenant

will not accept an alternative that would not be considered a Long Lead Item. Further, Landlord may not object to any items for which there is a long lead time in Tenant's Plans to the extent such items were included in the Interim Plans and not identified by Landlord as a Long Lead
Item. Landlord will also give to Tenant Landlord's good faith estimate of the period(s) of any delay which would be caused by any such Long Lead Item. Landlord shall not have the right to identify any Long Lead Items contained in or contemplated by the Interim Plans and Tenant's Plans after Landlord's Review Period for the Interim Plan and Tenant's Plans, as the case may be (other than in connection with a Change Proposal, as described below). Any unavailability or delay in obtaining any item contained in the Interim Plans or Tenant Plans which Landlord did not identify as a Long Lead Item prior to the end of Landlord's Review Period shall not constitute a delay due to Force Majeure and shall not excuse any delay or late delivery of the Premises or the Substantial Completion of Landlord's Work or Tenant's Work. Landlord,
Landlord's Contractor and Tenant shall cooperatively work in good faith to avoid the use of such Long Lead Items not identified in the Schematic Plans, and it shall be reasonable for Landlord to request that Tenant revise such aspects of the Tenant's Plans, unless the same were previously noted in the Schematic Plans, so as to avoid the use of such Long Lead Items; in furtherance of the foregoing, Tenant agrees that with regards to base building systems (such as plumbing, electrical and HVAC), the manufacturer from whom Landlord has acquired such base building
item shall, unless otherwise specifically identified in the Interim Plans or Tenant's Plans, be deemed acceptable for use in connection with Tenant's Work. Tenant shall have the right to
either (a) revise Tenant's Plans to eliminate any Long Lead Item(s), or (b) authorize Landlord to construct Tenant's Work in accordance with Tenant's Plans including any such Long Lead Items (any such approved Long Lead Items being hereinafter called "Tenant Approved Long Lead Items") and any delay resulting from the inclusion of such Tenant Approved Long Lead Items shall be a Tenant Delay without the need for any additional notice to Tenant. Unless Landlord shall have unconditionally approved all of the Interim Plans and Tenant's Plans, Tenant shall within five (5) Business Days after delivery of Landlord's response to the Interim Plans and within ten (10) Business Days after delivery of Landlord's response to Tenant's Plans, as applicable, deliver to Landlord such additional information, documentation and/or revisions to
the Interim Plans and/or Tenant's Plans as are necessary to obtain Landlord's approval thereof and this process shall continue until the Interim Plans and Tenant's Plans are approved by Landlord and Tenant. Tenant shall, promptly following approval of Tenant's Plans and Tenant's receipt of Landlord's request therefor, execute and deliver to Landlord any affidavits and documentation provided to Tenant by Tenant's architect and/or engineers preparing the TI Plans and required in order to obtain all permits and approvals necessary for Landlord to commence and complete Tenant's Work (excluding any operational permits that are required in order for Tenant to operate its business in the Premises, which such operational permits shall be Tenant's sole responsibility to obtain) on a timely basis ("Permit Documentation"). Time is of the essence in connection with Tenant's obligations under this Section 3.3.

(c) Concurrently with Landlord's review of Tenant's Plans, Landlord shall cause
Landlord's Contractor to solicit and obtain at least three (3) subcontractor bids for each trade and materials provider expected to cost in excess of Two Hundred Fifty Thousand and 00/100 Dollars ($250,000.00) ("Major Trade") in connection with Tenant's Work. Tenant shall have the right to propose one (1) subcontractor for each Major Trade and to consult with Landlord and
Landlord's Contractor regarding the preparation of the bid packages. All subcontractors shall be subject to Landlord's prior consent, which consent shall not be unreasonably withheld,

conditioned or delayed. Landlord and Landlord's Contractor shall involve Tenant (and Tenant's Construction Representative) in the preparation of the bid packages and the bidding process for each Major Trade, including reviewing with Tenant the bid packages and subcontractor responses and meeting with Tenant as reasonably requested by Tenant during such process. The bid packages shall require bids to identify all Long Lead Items and to specify estimated delivery dates therefor. Upon the conclusion of the bid solicitation process, Landlord shall deliver copies of the bids to Tenant (together with Landlord's designation of the bid Landlord intends to accept). Tenant shall reasonably cooperate with Landlord's efforts to expedite the bid process.

After receipt of the bids, Landlord shall have the right to select the subcontractor bids for Tenant's Work. Landlord shall reasonably consult with Tenant on the selection of the subcontractor bids for the Major Trades, but Landlord shall have the right, without obtaining
Tenant's approval, to select any subcontractor bids which Landlord deems to be qualified to perform the applicable portions of Tenant's Work, taking into consideration (i) Landlord's knowledge of the subcontractor project management staff for the subcontract in question, (ii) labor availability or capacity of the subcontractors in question to complete Tenant's Work by the Delivery Date, (iii) scheduling and availability of material and equipment to complete Tenant's Work by the Delivery Date.

After receipt of the bids and selection of the subcontractors, Landlord shall calculate and furnish to Tenant a "Total Costs Notice" for Tenant's Work which shall constitute the aggregate (the "Total TI Costs") of (i) the amounts payable under the subcontracts selected (and if and where Landlord's Contractor is performing work that would be performed by a subcontractor,
the cost of such work) in the bid process and broken down by trade ("Direct Costs"), (ii) an estimate of the Construction Management Fee (as hereinafter defined), (iii) the amount of
Landlord's Contractor's fee and indirect costs, and (iv) a reasonable construction contingency (not to exceed 3% of the Total Costs Notice amount) and a reasonable design contingency (not to exceed 10% of the Total Costs Notice amount) (collectively, the "Contingencies"). Landlord shall charge, as part of the Total TI Costs, a construction management fee (the "Construction Management Fee") for its management of Tenant's Work in an amount equal to three percent (3%) of the hard costs of Tenant's Work. The Construction Management Fee shall be paid from the Maximum Turnkey Amount as set forth in Section 3.6 below. In connection with the foregoing, Landlord and Tenant agree to use a Guaranteed Maximum Price contract for Tenant's Work and that Tenant's Work will be performed on an open book basis. Landlord shall provide Tenant with a copy, for informational purposes only, of the Guaranteed Maximum Price contract and any addendum thereto that is related to Tenant's Work.

Within ten (10) Business Days after Landlord's delivery of the Total Costs Notice (the "Initial Cost Approval Date"), Tenant may either approve the Total Costs Notice or provide changes to Tenant's Plans to eliminate or revise one or more scope-of-work items included in Tenant's Plans and request a revised Total Costs Notice. In the event that Tenant timely and properly requests such revised Total Costs Notice and submits changes to Tenant's Plans,
Landlord shall reprice Tenant's Plans for purposes of preparing a revised Total Costs Notice and deliver the revised Total Costs Notice within a reasonable time after such request and considering the scope of the changes proposed by Tenant. If Tenant fails to respond to the Total Costs Notice (either by approval of the Total Costs Notice or request for changes to Tenant's Plans) within such ten (10) Business Day period following delivery by Landlord, Tenant shall be

deemed to have approved the Total Costs Notice in its entirety; provided, however that no such automatic approval shall occur unless Landlord's submission contains the following notice (the "Deemed Approval Language"), printed in a prominent place on the outside thereof in not less fourteen (14) point bold-faced type: "**TENANT REVIEW REQUIRED; FAILURE TO RESPOND TO THIS SUBMISSION WITHIN TEN (10) BUSINESS DAYS SHALL RESULT IN AUTOMATIC APPROVAL PURSUANT TO LEASE SECTION 3.3(C)**". In addition, if Tenant's request for a revised Total Costs Notice results in the Total Cost Notice not being approved or deemed approved within ten (10) Business Days after the Initial Cost Approval Date (the "Final Cost Approval Date"), Tenant shall be deemed to have approved the Total Costs Notice in its entirety (subject to the inclusion of the Deemed Approval Language as set forth above). Tenant acknowledges and agrees that Tenant's approval or deemed approval of the Total Cost Notice authorizing Landlord to commence the performance of Tenant's Work by Final Cost Approval Date is a material condition to Landlord's ability to complete Tenant's Work by the Delivery Date. Once Tenant has approved the Total Costs Notice (or the Total Costs Notice is deemed approved), the parties shall promptly execute an instrument confirming the amount of the final Total Costs Notice. Notwithstanding the foregoing, the parties may elect to bid, award, and release Long Lead Items prior to the Final Cost Approval Date. In such event, any such bids, awards and release of Long Lead Items shall be deemed approved for purposes of the Total Costs Notice.

(d) Promptly following (i) approval of Tenant's Plans by Landlord, (ii) approval or deemed approval of the Total Costs Notice by Tenant, and (iii) receipt of a building permit from the City of Somerville, Landlord shall cause the work specified in Tenant's Plans, which shall include, but not be limited to, the work in the Work Matrix under the "Tenant" column ("Tenant's Work") to be performed in a good and workmanlike manner and in compliance with all applicable laws, codes and regulations. Tenant and Tenant's Construction Representatives, as defined in Section 3.9 below, shall have the right to observe the performance of Tenant's Work at reasonable times and upon reasonable prior notice to Landlord. In addition, commencing on the Date of this Lease Tenant shall have the right to have Tenant's Construction Representative attend all regularly scheduled weekly project meetings with Landlord's Contractor relating to Tenant's Work and the proposed construction schedule for Tenant's Work and, upon written request from Tenant, Landlord agrees to provide Tenant with updated copies of the construction schedule for Tenant's Work. Landlord's architect or Construction Representative shall prepare and distribute to Tenant's Construction Representative written minutes from such meetings.

Landlord agrees to prioritize the construction and delivery of the laboratory portions of the Premises and to use reasonable efforts to deliver the laboratory portions of the Premises to Tenant before the office portions of the Premises, so long as such efforts do not result in overall construction delays. Landlord shall thereafter prioritize delivery of the office portions of the Premises that directly support the laboratory uses. Upon Substantial Completion of Tenant's Work in the applicable portion(s) of the Premises, Tenant shall have the right to commence its operations in the laboratory portions of the Premises and, when available, the office portions of the Premises prior to the Commencement Date.

(e) Landlord agrees that the materials and equipment furnished in the performance of Landlord's Work and Tenant's Work will be free from defects not inherent in the quality described in the applicable plans and specifications therefor. Any portion of Landlord's Work or

Tenant's Work not conforming to the foregoing requirements will be considered defective. Landlord's warranty hereunder shall not apply to the extent of damage or defect caused by (i) the negligent acts or omissions or the willful misconduct of Tenant or anyone claiming under Tenant, (ii) improper operation by Tenant or anyone claiming under Tenant, or (iii) normal wear and tear and normal usage. The foregoing warranty with respect to each component of the Landlord's Work and Tenant's Work shall commence with respect to the Premises on the date on which Landlord has substantially completed the applicable component of Landlord's Work or Tenant's Work, as applicable, and shall expire on the date which is fifty-one (51) weeks after the commencement of the warranty on the applicable component of the Landlord's Work or Tenant's Work (the "Warranty Period"), and Tenant shall be required to deliver notice to Landlord of any defects prior to the expiration of the Warranty Period in order to permit Landlord to take action to enforce Landlord's warranty rights with respect to Landlord's Work and/or Tenant's Work, as applicable. Landlord agrees that it shall correct any portion of Landlord's Work and/or Tenant's Work, as the case may be, which during the applicable Warranty Period is found not to be in accordance with the warranties set forth in this Section 3.3(e). Subject to the foregoing and to the last paragraph of Section 3.2 above, Tenant shall be conclusively deemed to have accepted Landlord's Work and Tenant's Work unless, within the Warranty Period, Tenant gives Landlord a written notice setting forth in detail those portions of Landlord's Work or Tenant's Work Tenant does not accept. To the extent Tenant is responsible for the maintenance or repair of the equipment or mechanical items included within Tenant's Work, Landlord shall, to the extent assignable, assign the warranties relating to such equipment or mechanical items to Tenant; provided that if any such warranty may not be so assigned, Landlord will retain the same but will cooperate with Tenant, at Tenant's expense, in pursuing, in Landlord's name, any claim thereon which may arise while such warranty remains in effect.

(f) Tenant shall have the right, in accordance herewith, to submit for Landlord's approval written change proposals subsequent to Landlord's approval of the Tenant's Plans and Tenant's approval of the Total Costs Notice, if any (each, a "Change Proposal"). Any Change Proposal shall include fully detailed construction plans for the changes proposed to the Tenant's Plans. Provided the plans for such Change Proposal conform to the requirements of Exhibit C attached hereto, Landlord agrees to respond to any such Change Proposal within ten (10) Business Days after the submission thereof by Tenant, advising Tenant of any anticipated increase in costs ("TW Change Order Costs") to perform Tenant's Work associated with such Change Proposal, as well as an estimate of any delay which would likely result in the completion of Tenant's Work if a Change Proposal is made pursuant thereto ("Landlord's Change Order Response"). Notwithstanding the foregoing, Landlord will respond to any non-material Change Proposal within five (5) Business Days after submission thereof by Tenant. With respect to Change Proposals for which a response cannot reasonably be developed within five (5) Business Days, Landlord shall within the five (5) Business Day response period advise Tenant of the steps necessary in order for Landlord to evaluate the Change Order Proposal and the date upon which Landlord's Change Order Response will be delivered, which shall not exceed twelve (12) Business Days (provided, however, that Landlord shall use reasonable efforts to response within ten (10) Business Days). Tenant shall have the right within five (5) days after receiving Landlord's Change Order Response (or Landlord's notice that a Change Proposal could not be evaluated within the five (5) Business Day response period set forth above) to then approve or withdraw such Change Proposal. If Tenant fails to respond to Landlord's Change Order

Response within such five (5) day period, such Change Proposal shall be deemed withdrawn. If Tenant approves such Change Proposal, then such Change Proposal shall be deemed a "TW Change Order" hereunder and the TW Change Order Costs associated with the Change Order shall be deemed additions to the Total Costs Notice.

3.4 Substantial Completion. As used herein, the term "Substantially Complete", "Substantially Completed" or "Substantial Completion" shall mean the later to occur of (i) the substantial completion of construction of Landlord's Work and Tenant's Work, as certified by Landlord's architect, pursuant to and evidenced by a fully executed AIA G704 form signed by Landlord's General Contractor and Landlord's architect, with the exception of any Punch List Items (as defined below), and (ii) the issuance by the City of Somerville of a temporary or permanent certificate of occupancy or receipt of final approvals or signoffs for the Building and the Premises required for Tenant to lawfully operate in all of the Premises for the Permitted Uses. Landlord shall, until obtained, diligently pursue a permanent or final certificate of occupancy for the Premises if it shall not have received a certificate of occupancy by the date on which Landlord's Work and Tenant's Work are otherwise Substantially Complete. Notwithstanding the above, Landlord shall not be entitled to claim an extension of the date to Substantially Complete Landlord's Work or Tenant's Work (as applicable) due to delays caused by either Force Majeure or Tenant Delay unless Landlord shall have provided written notice to Tenant of the occurrence of such particular delay within seven (7) days of the date on which Landlord is aware of such particular delay. Landlord shall notify Tenant in writing when Landlord in good faith believes that Tenant's Work is Substantially Complete. Within three (3) Business Days after the giving of such notice to Tenant, Landlord, Landlord's architect, Tenant and Tenant's architect shall jointly inspect the Premises and develop the list of punch list items that can be completed without unreasonable interference with Tenant's use and occupancy of the Premises for the regular conduct of business ("Punch List Items"), provided that in the event of any dispute between Landlord and Tenant regarding whether or not Tenant's Work is Substantially Complete, or if Tenant or Tenant's architect shall fail to attend such inspection, the determination of Landlord's architect, acting reasonably, as to whether Tenant's Work is Substantially Complete, and any list of punch list items developed by Landlord and/or Landlord's architect, shall be final and binding on Landlord and Tenant. Landlord shall promptly complete all Punch List Items, at Landlord's sole cost and expense, and shall use reasonable efforts to complete all Punch List Items within thirty (30) days after the date of Substantial Completion.

3.5 Plans; Books and Records. From time-to-time during the construction of Landlord's Work directly affecting the Premises, Landlord shall allow Tenant's Construction Representative and such other representatives, contractors, agents and employees as Tenant deems advisable to review and make copies of plans and specifications (including all changes thereto) and generally to review the progress of all Landlord Work directly affecting the Premises (including the facilities and equipment serving the same). Such reviews shall be scheduled so as not to interfere with the conduct of Landlord's Work or Tenant's Work. Tenant shall be provided with copies of all changes or supplements to the construction plans for Landlord's Work directly affecting the Premises (including the facilities and equipment serving the same) when the same are given to Landlord's Contractor.

Landlord shall maintain full and detailed accounts, books and records including, without limitation, purchase orders, receipts, bids and subcontracts, on a discipline by discipline basis, for the costs of expenses relating to Tenant Work's with third party vendors and sub-contractors. Landlord shall provide Tenant with a final accounting (the "Final Accounting") in reasonable detail, together with all backup and supporting materials reasonably requested by Tenant, prepared by Landlord for all Direct Costs of Tenant's Work (including TW Change Order Costs and costs related to Tenant Delay) and other costs on the Total Costs Notice and Tenant will be permitted, upon request, to review all the backup and supporting materials. Landlord shall cause its contractors, architects, engineers and consultants to keep full and detailed accounts and exercise such controls as may be necessary for proper financial management of Tenant's Work. Tenant shall have the right to examine and copy all books and records referenced in this paragraph for up to seven (7) years from Substantial Completion of Tenant's Work, upon at least ten (10) Business Days prior written notice to Landlord.

3.6 Costs of the Plans and Tenant's Work. Tenant shall be responsible for all costs and expenses in connection with (i) preparing, revising and finalizing the Schematic Plans and Tenant's Plans, (ii) Tenant's security systems for the Premises, (iii) the purchase and installation of Tenant's audio-visual equipment for the Premises, and (iv) Tenant's furniture, fixtures and equipment for the Premises. Landlord agrees to pay the entire cost of Landlord's Work and Tenant shall not be liable therefor.

The cost of Tenant's Work shall be allocated as follows: The parties acknowledge that the Total TI Costs of Tenant's Work is anticipated to be $324.50 per square foot of Premises Rentable Area (the "Maximum Turnkey Amount"), as shown on the Preliminary Pricing schedule attached hereto as Exhibit A-6. If the Total TI Costs exceed the Maximum Turnkey Amount, then (i) to the extent that the increase in Total TI Costs is attributable to a change in the scope of Tenant's Work from that shown on or contemplated by the Schematic Plans or Work Matrix and/or to additional design elements, or a change to design elements, of Tenant's Work beyond those shown on or contemplated by the Schematic Plans or Work Matrix, then such increase in the Total TI Costs (i.e., the difference per square foot of Premises Rentable Area between the Total TI Costs per square foot of Premises Rentable Area and $324.50 per square foot of Premises Rentable Area) shall be Excess Costs (but shall not constitute a Tenant Delay) and shall be paid by first applying any unused amount, following the final determination of the costs of Tenant's Work, of the Contingencies and then paid by Tenant; and (ii) to the extent that the increase in costs is not attributable to a change in the scope of Tenant's Work from that shown on or contemplated by the Schematic Plans or Work Matrix and/or to additional design elements, or a change to design elements, of Tenant's Work beyond those shown on or contemplated by the Schematic Plans or Work Matrix, then such increase in the Total TI Costs (i.e., the difference per square foot of Premises Rentable Area between the Total TI Costs per square foot of Premises Rentable Area and $324.50 per square foot of Premises Rentable Area) shall be paid by Landlord. If the Total TI Costs per rentable square foot are less than the Maximum Turnkey Amount for any reason, then Annual Fixed Rent per square foot of Premises Rentable Area per annum as set forth in Section 1.1 above shall be decreased by the amount necessary to amortize such difference between $324.50 and the actual Total TI Costs on a rentable square foot basis over a seventy-two (72) month period with interest at the rate of eight percent (8%) per annum. For the avoidance of doubt, if the actual Total TI Costs as finally determined are $320.50 per rentable square foot, Annual Fixed Rent would be adjusted to

provide for a Financed Fit-Out Rent of $38.08 per rentable square foot per annum (as opposed to $38.92 per rentable square foot per annum), and the Financed Fit-Out Rent schedule set forth on Exhibit M shall be appropriately adjusted to reflect such change. Following completion of Tenant's Work and the final calculation of the Total TI Costs, Landlord shall deliver the Final Accounting to Tenant and the parties shall promptly execute an amendment to this Lease that makes such changes thereto as shall be required as a result thereof.

3.7 Tenant Delay; Force Majeure. A "Tenant Delay" shall be any actual delay in the Substantial Completion of Landlord's Work to the extent caused directly and solely by (i) Tenant's failure to submit Tenant's Interim Plans by the Design Submission Date and/or Tenant's Plans by the Plan Submission Date or to provide to Landlord any Permit Documentation required to be submitted in connection with the application for a building permit for Tenant's Work within the timeframes set forth herein for delivery of the same, (ii) any delay due to any Change Proposals or Tenant Approved Long Lead Items (except to the extent due to Landlord's or Landlord's Contractor's failure to timely order the Tenant Approved Long Lead Items or to the extent such Long Lead Items are included in or contemplated by the Schematic Plans or the Work Matrix) and any delays due to any errors, defects, discrepancies or inconsistencies in Tenant's Plans, (iii) failure of Tenant's Plans to comply with applicable laws, codes or regulations or any failure of Tenant or Tenant's architect to respond to requests within the time period set forth in this Article 3, (iv) any delay due to Tenant's or Tenant's vendors or contractors accessing the Premises or the Building prior to the Commencement Date (except as permitted in accordance with Section 3.8), provided, however, that the contractors performing Landlord's Work and Tenant's Work shall not be deemed to be Tenant's vendor or contractor, and any interference by Tenant or anyone acting under Tenant with the performance of Landlord's Work or Tenant's Work, (v) Tenant's failure to have completed the installation of its security systems, audio-visual equipment, furniture, and/or lab equipment prior to the date on which Landlord's Work and Tenant's Work would have been Substantially Complete but for such failure, or (vi) any other negligent or wrongful act or omission by Tenant, its employees, agents or contractors. The Delivery Date shall automatically be extended for the period of any delays caused by Tenant Delay(s) or Force Majeure so long as Landlord shall have provided written notice thereof to Tenant in a timely manner as provided in Section 3.1 above. Tenant shall pay to Landlord, as Additional Rent, the amount of any increase in the cost of Landlord's Work or Tenant's Work due to Tenant Delay (such amounts being the "Excess Costs") exceeds the unused Contingencies, within thirty (30) days after notice from Landlord given together with reasonable supporting documentation establishing such Excess Cost.

"Force Majeure" shall be defined as any strike or other labor trouble, fire, flood or other casualty, breakage, accident, repairs, unusually severe weather, governmental preemption of priorities or other controls in connection with a national or other public emergency, governmental moratoria, or inaction of governmental authority (or shortages of fuel, supplies or labor resulting therefrom), war, civil commotion, labor or transportation difficulties, inability to obtain supplies outside Landlord's or Tenant's reasonable control, or any other cause, whether similar or dissimilar, beyond Landlord's reasonable control; excluding, however, any financial difficulties.

The provisions of this Section 3.7 shall be subject to the second sentence of Section 3.4

3.8 Early Access. At such point as, in Landlord's reasonable judgment, Landlord's Work and Tenant's Work have proceeded to such point where Tenant may install its cabling, furniture, fixtures and equipment in the Premises without interfering with the performance of Landlord's Work or Tenant's Work (and provided Landlord shall have received a copy of each of Tenant's insurance policies or certificates of insurance therefor pursuant to Subsection 4.4
hereof), Landlord shall so notify Tenant and from and after such date of notification Tenant and its contractors shall have access to the Premises for the purposes of installing the same in preparation for Tenant's occupancy of the Premises; provided, however, that Landlord shall use reasonable efforts to provide Tenant and its contractors with such access at least sixty (60) days' prior to the date on which Landlord reasonably expects to achieve Substantial Completion of
Landlord's Work and Tenant's Work. In connection with such access, Tenant agrees (i) to cease promptly upon notice from Landlord any activity or work which has not been approved by Landlord (where such approval is required) or is not in compliance with the provisions of this
Lease or which shall interfere with or delay the performance of Landlord's Work or Tenant's Work, and (ii) to comply and cause its contractors to comply promptly with all reasonable procedures and regulations prescribed by Landlord from time to time for coordinating work being performed by Landlord and work being performed by Tenant, each with the other and with any other activity or work in the Building including, without limitation, the use of labor which shall work in harmony with all other contractors performing work at the Building. Such access by Tenant shall be deemed to be subject to all of the applicable provisions of this Lease as if the term had commenced, except that (i) there shall be no obligation on the part of Tenant solely because of such access to pay any Annual Fixed Rent or Additional Rent for Taxes or Operating Costs for any period prior to the Rent Commencement Date, and (ii) Tenant shall not be deemed thereby to have taken or accepted possession of the Premises or any portion thereof. If Tenant fails or refuses to comply or cause its contractors to comply with any of the obligations described or referred to above, then Landlord shall give written notice thereof to Tenant, and Tenant shall use diligent efforts to comply and cause its contractors to comply, and if such non-compliance is not cured within two (2) Business Days after Landlord's written notice to Tenant, Landlord may revoke Tenant's rights of access to the Premises until the Commencement Date.

3.9 Construction Representatives. Both Landlord and Tenant shall appoint one individual as its "Construction Representative" who is authorized to act on its behalf in
connection with any matters arising pursuant to this Article 3. The Construction Representative may be changed from time to time by notice hereunder from the then current Construction Representative to the other party's Construction Representative or by notice from Landlord or Tenant pursuant to Section 10.1. The initial Construction Representatives shall be Nat Wysor of Redgate (Landlord) and Steve Conti (Tenant). Notwithstanding Section 10.1, any notices or other communication under this Article 3 may be made by letter or other writing sent by U.S.
mail, facsimile or email, provided the communication is made by one party's Construction Representative to the other party's Construction Representative.

## Article 4

## Rent, Additional Rent, Insurance and Other Charges

4.1 The Annual Fixed Rent. Tenant shall pay Annual Fixed Rent to Landlord, or as otherwise directed by Landlord, without offset, abatement (except as provided in Sections 1.1

and 5.2 and Article 7), deduction or demand. Beginning on the Rent Commencement Date, Annual Fixed Rent shall be payable in equal monthly installments, in advance, on the first day of each and every calendar month during the term of this Lease, at the Account for Payment of Rent, or at such other place as Landlord shall from time to time designate by notice, by check drawn on a domestic bank.

The monthly payment of Annual Fixed Rent for any partial month at the expiration or earlier termination of the term of this Lease shall be prorated on a daily basis (based on a 30-day month), and if Annual Fixed Rent commences on a day other than the first day of a calendar month, the first monthly payment which Tenant shall make to Landlord shall be payable on the date Annual Fixed Rent commences and shall be equal to such pro-rated amount plus the monthly installment of Annual Fixed Rent for the succeeding calendar month.

Tenant shall have the right, in Tenant's sole discretion, and from time to time, to pre-pay all or any portion of the principal portion of the Financed Fit-Out Rent, without penalty, cost, fee or premium. The Financed Fit-Out Rent set forth in the table in Section 1.1 above was calculated by amortizing the principal amount of Seven Million Eight Hundred Seventy-Seven Thousand Three Hundred and 00/100 Dollars ($7,877,300.00) over a seventy-two (72) month period (such that the Financed Fit-Out Rent shall be payable during the Original Term only), commencing on the Rent Commencement Date, and such amortization was calculated on a monthly basis using an eight percent (8%) interest rate. Attached hereto as Exhibit M is the amortization schedule for the Financed Fit-Out Rent. Upon any partial prepayment of the principal portion of the Financed Fit-Out Rent, the Financed Fit-Out Rent for the remainder of the Original Term shall be recalculated by amortizing the remaining principal amount of the Financed Fit-Out Rent, after applying the amount of prepayment, over the remaining full calendar months in the Original Term, and such amortization shall be calculated on a monthly basis using an eight percent (8%) interest rate. For example, if Tenant makes a prepayment of $2,000,000 at the end of the twenty-fourth (24$^{th}$) month following the Rent Commencement Date (i.e., as of the end of Month 28 in the rent schedule set forth in Section 1.1), Annual Fixed Rent shall be adjusted, commencing as of Month 29 in the rent schedule set forth in Section 1.1, to provide for a Financed Fit-Out Rent of $25.16 per rentable square foot per annum (as opposed to $38.92 per rentable square foot per annum), and the Financed Fit-Out Rent schedule set forth on Exhibit M shall be appropriately adjusted to reflect such change. Within ten (10) Business Days after Tenant delivers a prepayment of the Financed Fit-Out Rent to Landlord, Landlord and Tenant shall enter into an amendment of this Lease memorializing the reduction in the amount of the Financed Fit-Out Rent and the Annual Fixed Rent. Within ten (10) Business Days after Tenant has paid the principal portion of the Financed Fit-Out Rent in full, Landlord and Tenant shall enter into an amendment of this Lease acknowledging that Tenant's obligation to pay the Financed Fit-Out Rent has been satisfied in full and the reduction in the Annual Fixed Rent.

4.2 Additional Rent. Commencing on the Rent Commencement Date, Tenant shall pay to Landlord, as Additional Rent, Tenant's Percentage of Taxes and Operating Costs as provided in Sections 4.2.1 and 4.2.2 and all other charges and amounts payable by or due from Tenant to Landlord (all such amounts referred to in this sentence being "Additional Rent"). If the Building becomes part of a larger development or project which has shared Operating Costs and/or Taxes, Operating Costs and/or Taxes, as applicable, attributable in part to the Building

and in part to other portions of such development or project shall be allocated to the Building and said other portions of the project or development an equitable basis.

4.2.1 Real Estate Taxes. Commencing on the Rent Commencement Date, Tenant shall pay to Landlord, as Additional Rent, Tenant's Percentage of Taxes (as hereinafter defined) assessed against the Property (or estimated to be due by governmental authority) for any Operating Year during the term of this Lease (Tenant's Percentage of Taxes being "Tenant's Tax Obligation").

Tenant shall pay to Landlord, as Additional Rent, commencing on the Rent Commencement Date and thereafter on the first day of each calendar month during the term but otherwise in the manner provided for the payment of Annual Fixed Rent, estimated payments on account of Tenant's Tax Obligation, such monthly amounts to be sufficient to provide Landlord by the time Tax payments are due or are to be made by Landlord a sum equal to Tenant's Tax Obligation, as reasonably estimated by Landlord from time to time on account of Taxes for the then current Operating Year. If the total of such monthly remittances for any Operating Year is greater than Tenant's Tax Obligation for such Operating Year, Landlord shall credit such overpayment against Tenant's subsequent obligations on account of Taxes (or promptly refund such overpayment if the term of this Lease has ended and Tenant has no further obligations to Landlord); if the total of such remittances is less than Tenant's Tax Obligation for such Operating Year, Tenant shall pay the difference to Landlord within thirty (30) days after being so notified by Landlord.

If, after Tenant shall have made all payments due to Landlord pursuant to this Subsection 4.2.1, Landlord shall receive a refund of any portion of Taxes as a result of an abatement of such Taxes by legal proceedings, settlement or otherwise (without either party having any obligation to undertake any such proceedings), Landlord shall pay or credit to Tenant Tenant’s Percentage of that percentage of the refund (after first deducting any expenses, including attorneys’, consultants’ and appraisers’ fees, incurred in connection with obtaining any such refund) which equals the percentage of the applicable Tax Year included in the term hereof, provided however, in no event shall Tenant be entitled to receive more than the sum of payments actually made by Tenant on account of Taxes with respect to such Tax Year.

In the event that the Rent Commencement Date shall occur or the term of this Lease shall expire or be terminated during any Tax Year, or should the Tax Year or period of assessment of real estate taxes be changed or be more or less than one (1) year, or should Tenant’s Percentage be modified during any Tax Year due to a change in the rentable area of the Building and/or the Premises or otherwise, as the case may be, then the amount of the monthly payment of Tax Excess which may be otherwise payable by Tenant as provided in this Subsection 4.2.1 shall be pro-rated on a daily basis based on a 30-day month.

“Taxes” shall mean all taxes, assessments, excises and other charges and impositions which are general or special, ordinary or extraordinary, foreseen or unforeseen, of any kind or nature which are levied, assessed or imposed by any governmental authority upon or against or with respect to the Property, Landlord or the owner or lessee of personal property used by or on behalf of Landlord in connection with the Property, or taxes in lieu thereof, and additional types of taxes to supplement real estate taxes due to legal limits imposed thereon. If, at any time, any

tax or excise on rents or other taxes, however described, are levied or assessed against Landlord, either wholly or partially in substitution for, or in addition to, real estate taxes assessed or levied on the Property, such tax or excise on rents from the Property shall be included in Taxes; however, Taxes shall not include franchise, estate, inheritance, income (except to the extent that a tax on income or revenue is levied solely on rental revenues and not on other types of income and then only from rental revenue generated by the Property) or capital levy taxes assessed on Landlord. Taxes also shall include all reasonable, out-of-pocket court costs, attorneys', consultants' and accountants' fees, and other expenses reasonably incurred by Landlord in connection with any efforts to obtain abatements or reduction of Taxes for any year within the Term. Landlord shall account for such expenses and for any reduction in Taxes in the year in which such expenses were incurred or the year in which such tax reduction was granted, as applicable, and if such reduction affects more than one (1) year, the expenses shall be amortized over each year for which a reduction is granted. Taxes shall include any estimated payment made by Landlord on account of a fiscal tax period for which the actual and final amount of taxes for such period has not been determined by the governmental authority as of the date of any such estimated payment.

4.2.2 Operating Costs. Commencing on the Rent Commencement Date, Tenant shall pay to Landlord, as Additional Rent, Tenant's Percentage of all Operating Costs, as hereinafter defined, paid or incurred by Landlord with respect to the Property in any twelve-month period established by Landlord (an "Operating Year") during the term of this Lease (Tenant's Percentage of Operating Costs being "Tenant's Operating Cost Obligation"). Tenant shall pay to Landlord, as Additional Rent, commencing on the Rent Commencement Date and thereafter on the first day of each calendar month during the term but otherwise in the manner provided for the payment of Annual Fixed Rent, estimated payments on account of Tenant's Operating Cost Obligation, such monthly amounts to be sufficient to provide to Landlord, by the end of each Operating Year, a sum equal to Tenant's Operating Cost Obligation for such Operating Year, as estimated by Landlord from time to time. Within one hundred twenty (120) days after the end of each Operating Year during the term, Landlord shall furnish to Tenant an itemized statement setting forth the amount of Operating Costs for the preceding Operating Year and a computation of Tenant's Operating Cost Obligation, prepared and computed in accordance with then prevailing customs and practices of the real estate industry, consistently applied. Any such year-end statement by Landlord relating to Operating Costs shall be final and binding upon Tenant unless it shall give a Tenant's Audit Notice, as defined below. If, at the expiration of each Operating Year in respect of which monthly installments on account of Tenant's Operating Cost Obligation shall have been made as aforesaid, the total of such monthly remittances is greater than Tenant's Operating Cost Obligation for such Operating Year, Landlord shall credit such overpayment against Tenant's subsequent obligations on account of Operating Costs (or promptly refund such overpayment if the term of this Lease has ended and Tenant has no further obligation to Landlord); if the total of such remittances is less than Tenant's Operating Cost Obligation for such Operating Year, Tenant shall pay the difference to Landlord within thirty (30) days after being so notified by Landlord.

Any cost not included in a year-end statement of Operating Costs (each an "Omitted Cost") within twenty-four (24) months of the date any such Omitted Cost has been incurred shall not be payable by Tenant. Further, if (a) such Omitted Cost is a capital item subject to amortization as provided below, the Omitted Cost will be amortized over the remainder of the

useful life of such capital items, and (b) such Omitted Cost is not a capital item subject to amortization and the amount of the Omitted Cost exceeds $25,000.00, one-half (1/2) of such Omitted Cost shall be due from Tenant over each of the next two (2) Operating Years, without interest.

In the event that the Rent Commencement Date shall occur or the term of this Lease shall expire or be terminated during any Operating Year or Tenant's Percentage shall be modified during any Operating Year due to a change in the rentable area of the Building and/or the Premises or otherwise, as the case may be, then the monthly payment amount of Operating Cost Excess which may be payable by Tenant as provided in this Subsection 4.2.2 shall be pro-rated on a daily basis based on a 30-day month.

"Operating Costs" shall include, without limitation, all reasonable costs and expenses paid or incurred for the operation, cleaning, management, maintenance, repair, upkeep and security of the Property, including, without limitation:

(i) all salaries, wages, fringe benefits, payroll taxes and workmen's compensation insurance premiums related thereto and all other costs paid or incurred with respect to employment of personnel engaged in operation, administration, cleaning, maintenance, repair, upkeep and security of the Property (but only at the level of General Manager and below) including, without limitation, supervisors, property managers, accountants, bookkeepers, janitors, carpenters, engineers, mechanics, electricians and plumbers;

(ii) all utilities and other costs related to provision of heat (including oil, steam and/or gas), electricity, air conditioning, and water (including sewer charges) and other utilities to the Property (exclusive of reimbursement to Landlord for any of same received as a result of direct billing to any tenant of the Building);

(iii) all costs, including supplies, material and equipment costs, for cleaning and janitorial services to the Property, the Building and, if applicable, adjacent walks and ways (including, without limitation, trash removal and interior and exterior window cleaning), and interior and exterior landscaping and pest control (but excluding any cleaning, janitorial and trash removal services for individual tenant spaces that is not performed for all tenants);

(iv) the cost of replacements for tools and other similar equipment used in the repair, maintenance, cleaning and protection of the Property, provided that, in the case of any such equipment used jointly on other property of Landlord, such costs shall be suitably prorated among the Property and such other properties;

(v) all costs and premiums for fire, casualty, rental income, liability and such other insurance as may be maintained from time to time by Landlord

relating to the Property and premiums for fidelity bonds covering persons having custody or control over funds or other property of Landlord relating to the Property;

(vi) all costs of maintaining, repairing, decorating, operating, administering, inspecting and protecting the Property (including, without limitation, lighting, installation, maintenance, repair and alteration of signs, snow removal on the Property and adjacent walks and ways, paving, patching and restriping of parking areas and operation, maintenance, replacement (subject to the limitation on capital expenditures below) and repair of heating, ventilating and air conditioning equipment, fire protection and security systems, elevators, roofs, parking areas and any other common Building equipment, systems or facilities), and all costs of structural and other repairs and replacements (other than repairs which are reimbursable from contractors, insurance, other tenants of the Building or from others and other than repairs excluded from Operating Costs as provided below) necessary to keep the Property in good working order, repair, appearance and condition;

(vii) costs of compliance (but with respect to capital expenditures subject to the limitation below) with any laws, rules, regulations, ordinances, agreements (including, without limitation, the Mobility Management Plan (as defined in Subsection 6.1.2 below) and any similar plans and agreements) or standards applicable to the Building or the Property, which conformance is not the responsibility of any tenant of the Building, and which Landlord elects or is required to perform;

(viii) all costs incurred in connection with the administration and supervision of all matters referred to in items (a) through (g) hereof and in performing Landlord's obligations under Article 5, including Landlord's office overhead costs provided that, if any such administrative or supervisory personnel are also employed on other property of Landlord, such cost of compensation shall be suitably prorated among the Property and such other properties; and

(ix) management fee of up to three (3%) percent of base rents (excluding any component of base rents that is expressly attributable to leasehold improvements or construction allowances or the cost of Landlord's construction obligations including, but not limited to, the Financed Fit-Out Rent) payable by tenants of the Property.

If, during the term of this Lease, Landlord, in its sole discretion, installs a new or replacement capital item for the purpose of (i) complying with any law, rule, regulation, order or ordinance, or any amendment thereto or interpretation thereof, first enacted after the Commencement Date or (ii) reducing (or avoiding increases in) Operating Costs otherwise relating to the operation of the Building, the cost of such item amortized on a straight line basis over its useful life and in accordance with generally accepted accounting principles ("GAAP")

with interest at the “Prime Rate” (as published in the Wall Street Journal or comparable financial publication reasonably selected by Landlord) plus two percent (2%) shall be included in Operating Costs; provided, however, that the annual amortized costs of the capital item in clause
(ii) of this sentence included in Operating Costs shall not exceed the actual annual savings resulting from such expenditure. Notwithstanding the foregoing, replacements of the structural elements of the Building (including the Parking Facility, as defined in Section 5.5 below) including the roof, structural columns, floor slabs and exterior walls thereof, which replacements would properly be categorized as capital expenditure according to generally accepted accounting principles, shall not be included in Operating Costs.

Notwithstanding the foregoing or anything to the contrary herein, Operating Costs shall not include (i) any costs or expenses incurred by Landlord in the construction and development of the Building, including construction for tenants and/or costs to prepare, renovate, repaint, redecorate or perform any other work in any space leased to an existing tenant or prospective tenant of the Building; (ii) payments of principal, interest or other charges on mortgages;
(iii) costs for categories of services provided to other tenants but not to Tenant and the costs of any subsidies provided to any other tenants that are not provided to Tenant; (iv) intentionally omitted; (v) costs incurred in connection with the making of repairs or replacements which are the obligation of another tenant or occupant of the Building; (vi) advertising, marketing, promotional, public relations or brokerage fees, commissions or expenditures; (vii) interest or penalties for any failed or untimely payments by Landlord under any contract or agreement;
(viii) costs (including, without limitation, attorneys’ fees and disbursements) incurred in connection with any judgment, settlement or arbitration award resulting from any gross negligence or willful misconduct of Landlord or its agents; (ix) costs of electricity or utilities furnished directly to any premises of other tenants of the Building where such utility is separately metered to such premises or such tenant pays a separate charge therefor; (x) costs incurred in connection with Landlord’s preparation, negotiation, dispute resolution and/or enforcement of leases, including court costs and attorneys’ fees and disbursements in connection with any summary proceeding to dispossess any other tenant, or incurred in connection with disputes with prospective tenants, leasing agents, purchasers or mortgagees; (xi) costs of repairs, restoration or replacements occasioned by fire or other casualty, or caused by the exercise of the right of eminent domain (other than commercially reasonable deductibles or commercially reasonable self-insured retention amounts, which amounts shall be included in Operating Costs);
(xii) legal and other professional fees relating to matters which are excluded from Operating Costs for the Building; (xiii) costs to make improvements, alterations and additions to the Building which are required in order to remedy violations of laws, rules, orders, regulations and/or directives that existed on the Commencement Date; (xiv) depreciation; (xv) amounts other than the management fee specified above paid to subsidiaries or Affiliates of Landlord for services rendered to the Building to the extent such amounts exceed the competitive costs for delivery of such services were they not provided by such related parties; (xvi) expenditures for new or replacement capital items other than those which are expressly permitted above; (xvii) expenses incurred by Landlord in connection with any financing, sale or syndication of the Building or any portion thereof; (xviii) interest, principal, points and fees, amortization or other costs associated with any debt and rent payable under any lease to which this Lease is subject and all costs and expenses associated with any such debt or lease and any ground lease rent, irrespective of whether this Lease is subject or subordinate thereto; (xix) expenditures for the replacement of any item covered by installation of or any warranty (to the extent of the coverage

of such warranty); (xx) costs to correct any penalty or fine incurred by Landlord due to Landlord's or its employees, agents or contractors violation of any federal, state, or local law or regulation and any interest or penalties due for late payment by Landlord of any of the Operating Costs; (xxi) the wages of any employee for services not related directly (in whole or part) to the management, maintenance, operation and repair of the Building provided that if such employee is also employed on other property of Landlord, such wages shall be suitably prorated among the Building and such other properties; (xxii) Landlord's general corporate overhead and administrative expenses except to the extent related to the Building; (xxiii) reserves; (xxiv) costs to the extent that another party compensates or pays so that Landlord shall not recover any item of cost more than once; (xxv) costs of correcting any latent defects or original design defects in the Building's construction, materials, or equipment during the Original Term, Landlord agreeing to use reasonable efforts to determine whether any required repairs are due to latent defects or original design defects; (xxvi) costs of correcting any damage caused by any subway or mass transit line; (xxvii) cost of any repair, replacement or correction due to the Building, including but not limited to the roof and the foundation, not being in good condition and repair as of the Commencement Date; and (xxviii) the cost of investigating or monitoring of site conditions, repair cleanup, containment, remediation, removal or restoration work or detoxification of the Property as provided in Section 5.6 below. In addition, and notwithstanding anything to the contrary herein, Tenant shall not be responsible for any Operating Costs that are specifically incurred in connection with subsidizing, improving, installing, managing, operating, maintaining, repairing or replacing any components of the Building (including the Common Areas) that are dedicated exclusively to retail use.

In addition, if during any portion of any Operating Year for which Operating Costs are being computed, less than ninety-five percent (95%) of the rentable area of the Building was leased to tenants or if Landlord is supplying less than ninety-five percent (95%) of the rentable area of the Building with the services and utilities being supplied hereunder, Landlord may, at its option, reasonably project, on an item-by-item basis, consistently applied, the Operating Costs that would have been incurred if ninety-five percent (95%) of the Building were occupied for such Operating Year and such services and utilities were being supplied to ninety-five percent (95%) of the rentable area of the Building, and such projected amount shall, for the purposes hereof, be deemed to be the Operating Costs for such Operating Year.

Upon the written request of Tenant ("Tenant's Audit Notice"), and provided Tenant shall have paid all amounts invoiced by Landlord on account of Operating Costs for the applicable Operating Year, Tenant shall have the right to examine Landlord's books and records applicable to Operating Costs for such Operating Year, provided such review is commenced within one hundred and twenty (120) days of Tenant's receipt of Landlord's final statement of Operating Costs for the applicable Operating Year (the "Final Statement") and thereafter undertaken by Tenant or its accountants (provided such accountants are compensated (i) at an hourly rate, (ii) on a flat fee basis or (iii) on contractual basis where one-half (1/2) of the fee is on a flat fee basis and one-half (1/2) of the fee is on a contingency fee basis where such contingency fee does not exceed 200% of the flat fee) with due diligence. Such right to examine the records shall be exercisable upon reasonable advance notice to Landlord and at reasonable times during Landlord's business hours. If Tenant objects to Landlord's accounting of any Operating Costs, Tenant shall, on or before the date one hundred and eighty (180) days following receipt of the Final Statement, notify Landlord that Tenant disputes the correctness of such accounting,

specifying the particular line items which Tenant claims are incorrect otherwise, Tenant shall be deemed to have waived any and all objections to such Final Statement. Tenant shall pay all costs of the audit, provided, however, if it is determined that Tenant overpaid Additional Rent for Operating Costs by more than four percent (4%) for the year in question, Landlord shall reimburse Tenant for all reasonable costs of the audit, not to exceed Ten Thousand Dollars and 00/100 ($10,000.00) for a particular audit, and the amount of the overcharge shall be credited against Tenant's next payment of Operating Costs (or refund such amount to Tenant within thirty (30) days if the Term has ended and Tenant has no further obligations to under this Lease). If the audit shall determine that Tenant was undercharged for the Landlord's Operating Costs, Landlord may invoice Tenant for such amount and Tenant shall pay the amount of such undercharge to Landlord within thirty (30) days after receipt of such invoice. If the audit shows that Tenant overpaid Additional Rent for Operating Costs by more than four percent (4%), Tenant shall have the right to review and audit Operating Costs for the prior three (3) years.

4.3 Personal Property and Sales Taxes. Tenant shall pay all taxes charged, assessed or imposed upon the personal property of Tenant and all taxes on the sales of services or inventory, merchandise and any other goods by Tenant in or upon the Premises.

4.4 Insurance.

4.4.1 Insurance Policies. Tenant shall, at its sole cost and expense, take out and maintain, or cause to be maintained, throughout the term of this Lease or as otherwise included in this Section 4.4 or as otherwise noted in this Lease, the following insurance:

4.4.1.1 Commercial general liability covering the Premises, insuring Tenant against any liability arising out of the use, occupancy, or maintenance of the Premises, with such insurance written on an ISO occurrence form CG 00 01 04 13 (or a substitute form providing equivalent coverage) including coverage for broad form contractual liability (which shall include coverage for Tenant's indemnification obligations under this Lease), bodily injury (including death and mental anguish), third-party property damage, fire legal liability, host liquor liability, premises and operations. The minimum limits of insurance shall be no less than $1,000,000 per occurrence, $2,000,000 general aggregate, and $1,000,000 personal and advertising injury, with such per occurrence and general aggregate limits applying on a per location basis, and with such coverage including Tenant as a Named Insured. Landlord, Landlord's Agent, and the holder of any mortgage on the Premises or Property, as set out in a notice from time to time, along with Landlord's and Landlord's Agents' directors, officers, principals, members, partners, shareholders, employees, successors, and assigns (collectively, including Landlord, "Landlord Insureds") shall be named as additional insureds as their interests may appear. Such additional insured status must be afforded to the fullest extent permitted by law by way of the ISO CG 20 11 04 13 endorsement (or its equivalent). Such insurance shall include a separation of insureds endorsement, shall be primary and not contributing with or in excess of coverage that the Landlord or Landlord Insureds may carry, and shall be endorsed to provide a waiver of subrogation in favor of the Landlord Insureds by means of the ISO CG 24 04 endorsement (or its equivalent). No policy maintained by Tenant under this Section 4.4.1 shall contain a deductible greater than $5,000;

4.4.1.2 Products and completed operations insurance with aggregate limits of $10,000,000. Such insurance shall include the Landlord Insureds as an additional insured and shall provide a waiver of subrogation in favor of the Landlord. Such insurance shall be maintained for a period of time under which a claim may be properly asserted under the applicable statute of limitations or repose;

4.4.1.3 Worker's compensation insurance with statutory limits covering all of Tenant's employees working on the Premises and employer's liability insurance with minimum limits of $1,000,000 each employee per accident, $1,000,000 each employee by disease, and $1,000,000 policy limit by disease and such insurance shall include a waiver of subrogation in favor of the Landlord Insureds;

4.4.1.4 Property insurance on a "replacement cost" basis with an agreed value endorsement covering all of Tenant's personal property, including, but not limited to, furniture, furnishings, fixtures and equipment and other personal property located at the Premises or otherwise brought to the Premises by Tenant and anyone acting under Tenant, (collectively, Tenant's Property) and any improvements and betterments that
Tenant ("Tenant's Improvements") makes to the Premises after taking possession of Premises. Such insurance shall be written on a special cause of loss property insurance form. Such insurance shall include coverage for sprinkler leakage, leakage from any window or sill, and water damage, including bursting, leakage, or stoppage of any pipes, provided that such coverage is commercially available and Landlord does not otherwise approve Tenant's insurance without such coverage. Such insurance shall not include a deductible of greater than $10,000 unless otherwise approved by Landlord. In the event of a loss at the Premises whereby Tenant's Improvements are damaged, Tenant shall use any applicable insurance proceeds for the repair or replacement of the Tenant's Improvements at the Premises. The Landlord shall have no interest in the insurance covering the Tenant's Property and will not carry insurance on the Tenant's Property; however, Landlord will sign all documents reasonably necessary in connection with the settlement of any claim or loss on behalf of the Tenant;

4.4.1.5 Business income and extra expense insurance covering no less than twelve months of Rent payable by Tenant under this lease, with such coverage including a 365- day extended period of indemnity endorsement;

4.4.1.6 Commercial automobile insurance with limits of $1,000,000 combined single limit covering losses for bodily injury and property damage, for all owned, hired & nonowned vehicles. Landlord shall not be held responsible for any physical damage sustained by the vehicles while parked on or around the Property;

4.4.1.7 Umbrella / excess liability insurance, written on a follow-form basis in excess of the commercial general liability, commercial automobile liability, and employers liability insurance required herein with minimum limits of $10,000,000 per occurrence and $10,000,000 general aggregate. Such insurance shall not be more restrictive than the underlying applicable insurance policy and must not include any exclusion or limitation that the coverage provided by such policy is primary to, and non-contributory with, any other insurance of Landlord Insureds, whether such other

insurance is primary, excess, self insurance, or on any other basis. Said umbrella / excess liability coverage must be vertically exhausted where it is not subject to any "other insurance" provision under Tenant's commercial general liability, commercial automobile liability, employers liability, or umbrella / excess insurance policies;

4.4.1.8 Employment practices liability insurance with minimum limits of $1,000,000 per claim and in the annual aggregate, providing coverage for employment- related claims made by employees and by third parties, with third party coverage provided by endorsement, including, but not limited to, claims for discrimination, wrongful termination, and harassment. Said policy must include full prior acts coverage or a retroactive date not later than the date of the Lease; and

4.4.1.9 Such other insurance, in such amounts, as Landlord shall determine are customarily carried in the area in which the Property is located for premises similar to the Premises which are used for similar purposes and which are located in properties comparable to the Building.

4.4.2 Requirements. All policies of insurance required in this Lease and maintained by Tenant shall contain deductibles and self-insured retentions not in excess of that reasonably approved by Landlord, or as otherwise required herein or approved by Landlord, and no Landlord Insureds will be responsible for any deductible or self-insured retentions under insurance policies maintained by the Tenant. All such policies of insurance required in this Lease shall be primary and noncontributory with respect to any insurance policies carried by Landlord or Landlord Insureds, whether by such language being specifically included or endorsed under the policy or otherwise, and such policies shall be obtained from insurers qualified to do business and in good standing in the Commonwealth of Massachusetts having a rating by A.M. Best Company of at least A-VIII or otherwise be acceptable to Landlord. Tenant shall, prior to the Commencement Date and thereafter, not less than ten (10) days prior to any policy expiration, deliver to Landlord a certificate of the insurance, representing that such policy has been issued and providing the coverage required by this Section and containing provisions specified herein. Tenant shall also deliver to Landlord copies of paid invoices or paid receipts of the policies required in this Section no later than thirty (30) days after the renewal date. Each such policy required in this Section shall include a notice of cancellation endorsement in favor of the Landlord, whereby Landlord shall be notified of cancellation of any policies with at least thirty (30) days prior written notice thereto, with the exception of ten (10) days for non-payment of premium. If any such notice of cancellation endorsement is not commercially available, then Tenant shall endeavor to provide Landlord with such notice. Any insurance required of Tenant under this Lease may be furnished by Tenant under a blanket policy carried by it provided that such blanket policy shall reference the Premises, shall guarantee a minimum limit available for the Premises equal to the insurance amounts required in this Lease, and shall provide coverage that is no less than what would otherwise be afforded to the Premises on a standalone policy of insurance that is only applicable to covering the Premises. Tenant shall provide Landlord with copies of all endorsements required in this Lease upon thirty (30) days written notice from Landlord. The failure of Landlord to demand evidence of insurance or to identify any deficiency in any insurance coverage required in this Lease will not be construed as a waiver by Landlord of Tenant's obligation to comply with the insurance requirements of this Lease. If Tenant does not comply with any of the insurance requirements of this Lease, whether in Subsection 4.4.1,

Subsection 4.4.2, or otherwise, Landlord shall provide Tenant with at least fifteen (15) days written notice of such non-compliant coverage. If Tenant does not provide Landlord with evidence of coverage for any non-compliant coverage, then Landlord may, at its' option and at Tenant's expense, purchase such insurance coverage that is not compliant with the Lease.
Should Tenant at any time maintain higher limits than the minimum limits required herein, such higher limits shall be deemed required by this Lease for so long as such higher limits are maintained.

4.4.3 Vendors Insurance. In addition to the insurance Tenant is required to maintain under this Lease, Tenant shall require its vendors, consultants, and contractors entering the Building to maintain such insurance as Landlord shall reasonably determine to be necessary, and satisfactory evidence of such insurance must be delivered to Tenant prior to entry into the Building by such vendors, consultants, and contractors. Tenant shall have a written agreement with all vendors, consultants, and contractors in connection with the work or services to be performed at the Premises. Said agreement shall require each vendor, consultant, and contractor to provide certificates of insurance to Tenant promptly after Tenant's request, and Tenant shall deliver the same to Landlord within five (5) business days after Landlord's request.

4.4.4 Waiver of Subrogation. Subject to the foregoing provisions of this Subsection 4.4.4, and insofar as may be permitted by the terms of the property insurance policies carried by it, each party hereby releases the other with respect to any claim which it might otherwise have against the other party for any loss or damage to its property to the extent such damage is actually covered or would have been covered by policies of property insurance required by this Lease to be carried by the respective parties hereunder. In addition, Tenant agrees to exhaust any and all claims against its insurer(s) prior to commencing an action against Landlord for any loss covered by insurance required to be carried by Tenant hereunder.

Landlord and Tenant hereby waive and shall cause their respective insurance carriers to waive any and all rights of recovery, claims, actions or causes of action against the other for any loss or damage to person with respect to Tenant's property, any leasehold improvements, the Building, the common areas of the Building, the Premises, or any contents thereof, including rights, claims, actions and causes of action based on negligence, which loss, damage or injury is (or would have been, had the insurance required by this Lease been carried) covered by insurance.

4.5 Utilities. Tenant shall during the term pay all (i) utility charges for those utilities to the Premises which are separately metered based on actual usage, and (ii) utility charges allocable to the Premises, without mark-up, for those utilities to the Premises which are submetered, and (iii) all charges for telephone and other services not supplied by Landlord pursuant to Subsections 5.1.1 and 5.1.2, whether designated as a charge, tax, assessment, fee or otherwise, all such charges to be paid as the same from time to time become due. Except as otherwise provided in this Section 4.5 or in Article 5, it is understood and agreed that Tenant shall make its own arrangements for the installation or provision of all utilities and services and that Landlord shall be under no obligation to furnish any utilities to the Premises.

Tenant acknowledges that Annual Fixed Rent does not include the cost of supplying utilities to the Premises. The Premises shall, as part of Tenant's Work, be separately metered for

electricity and Tenant shall contract directly with the public utility for a supply of electricity to the Premises and shall pay all bills therefor when due.

Tenant shall pay as Additional Rent all cost of water and gas supplied to the Premises as determined by Landlord by submetering or similar device and the cost of installing, operating, maintaining and repairing any meter or other device used to measure Tenant's water and gas consumption and any cost incurred by Landlord in keeping account of or determining Tenant's water and gas consumption. Alternatively, at Landlord's option, Tenant shall pay Tenant's Percentage of the charges for water and gas allocable to those portions of the Building leased or intended to be leased to tenants, within ten days of invoice therefor, provided however if some or all of the areas leased or intended to be leased to tenants are separately metered for water and/or gas, such Tenant's Percentage for purposes of this Section 4.5 only shall be determined by dividing the rentable area of the Premises by the rentable area of the portions of the Building not separately metered for water and/or gas consumption, as the case may be.

4.6 Late Payment of Rent. If any installment of Annual Fixed Rent or any Additional Rent is not paid within five (5) days after the date the same is due, it shall bear interest (as Additional Rent) from the date due until the date paid at the Default Rate (as defined in Section 8.4). In addition, if any installment of Annual Fixed Rent or Additional Rent is unpaid for more than five (5) days after the date due, Tenant shall pay to Landlord a late charge equal to the greater of One Hundred Dollars ($100) or four percent (4%) of the delinquent amount. The parties agree that the amount of such late charge represents a reasonable estimate of the cost and expense that would be incurred by Landlord in processing and administration of each delinquent payment by Tenant, but the payment of such late charges shall not excuse or cure any default by Tenant under this Lease. Absent specific provision to the contrary, all Additional Rent shall be due and payable in full thirty (30) days after demand by Landlord. Notwithstanding the foregoing, Landlord shall waive the aforesaid late charge as to any such late payment so long as there is not a Default of Tenant and such payment is made within five (5) Business Days following any required written notice to Tenant that such payment is past due and Tenant has not been more than five (5) Business Days late in paying any other amount due Landlord hereunder more than once within the calendar year in which such late payment has occurred.

4.7 Security Deposit. Within ten (10) Business Days following the execution of this Lease, Tenant shall deposit with Landlord the Security Deposit. The Security Deposit shall be held by Landlord as security for the faithful performance of all the terms of this Lease to be observed and performed by Tenant. The Security Deposit shall not be mortgaged, assigned, transferred or encumbered by Tenant and any such act on the part of Tenant shall be without force and effect and shall not be binding upon Landlord. Tenant shall cause the Security Deposit to be maintained throughout the term in the amount set forth in Section 1.1. Provided that as of the second (2nd) anniversary of the Commencement Date there are no uncured Defaults of Tenant under this Lease, the Security Deposit shall be reduced to by one-half such that it shall be equal to three (3) months of the Base Rent due per month for Months 5-16 as set forth in the schedule in Section 1.1, as the same may have been adjusted pursuant to Section 3.6 (leaving the Security Deposit at an amount equal to three (3) months of the Base Rent due per month for Months 5-16 as set forth in the schedule in Section 1.1). If Tenant shall be entitled to a reduction in the Security Deposit as aforesaid, Tenant may deliver either an amendment to the Letter of Credit or a new Letter of Credit in the amount of then applicable Security Deposit.

If the Annual Fixed Rent or Additional Rent payable hereunder shall be overdue and unpaid or should Landlord make any payment on behalf of the Tenant, or Tenant shall fail to perform any of the terms of this Lease, then Landlord may, at its option and without notice or prejudice to any other remedy which Landlord may have on account thereof, appropriate and apply the entire Security Deposit or so much thereof as may be necessary to compensate Landlord toward the payment of Annual Fixed Rent, Additional Rent or other sums or loss or damage sustained by Landlord due to such breach by Tenant, provided that Landlord shall not appropriate and apply the Security Deposit on account of any breach of this Lease by Tenant unless Tenant's breach of this Lease shall have ripened into a Default of Tenant (i.e. after any applicable notice and expiration of any applicable cure period); and Tenant shall forthwith upon demand restore the Security Deposit to the amount stated in Section 1.1. Notwithstanding the foregoing, upon the application by Landlord of all or any portion of the Security Deposit (with or without notice thereof to Tenant) to compensate Landlord for a failure by Tenant to pay any Annual Fixed Rent or Additional Rent when due or to perform any other obligation hereunder, and until Tenant shall have restored the Security Deposit to the amount required by Section 1.1, Tenant shall be deemed to be in default in the payment of Additional Rent for purposes of Section 8.1(a)(I) hereof. So long as Tenant shall not be in default of its obligations under this Lease, Landlord shall return the Security Deposit, or so much thereof as shall have not theretofore been applied in accordance with the terms of this Section 4.7 (and less any amounts Landlord shall estimate shall be due from Tenant following year-end reconciliation of Operating Costs and Taxes) to Tenant within thirty (30) days following the expiration or earlier termination of the term of this Lease and the surrender of possession of the Premises by Tenant to Landlord in accordance with the terms of this Lease. While Landlord holds the Security Deposit, Landlord shall have no obligation to pay interest on the same and shall have the right to commingle the same with Landlord's other funds, provided that Landlord keeps an accounting of the Security Deposit. If Landlord conveys Landlord's interest under this Lease, the Security Deposit, or any part thereof not previously applied, shall be turned over by Landlord to Landlord's grantee, and Tenant shall look solely to such grantee for proper application of the Security Deposit in accordance with the terms of this Section 4.7 and the return thereof in accordance herewith. The holder of a mortgage on the Property shall not be responsible to Tenant for the return or application of the Security Deposit, whether or not it succeeds to the position of Landlord hereunder, unless such holder actually receives the Security Deposit.

Tenant shall post the Security Deposit in the form of a letter of credit (the "Letter of Credit") (which shall be in the form attached as Exhibit K or such other form reasonably approved by Landlord, which approval shall not be unreasonably withheld, conditioned or delayed, and which satisfied the requirements of this paragraph), which shall (a) be unconditional and irrevocable and otherwise in form and substance reasonably satisfactory to Landlord; (b) permit multiple draws; (c) be issued by a commercial bank reasonably acceptable to Landlord from time to time; (d) be made payable to, and expressly transferable and assignable at no charge by, Landlord; (e) be payable at sight upon presentment of a sight draft accompanied by a certificate of Landlord stating either that there is a Default of Tenant or that Landlord is otherwise permitted to draw upon such Letter of Credit under the express terms of this Lease, and the amount that Landlord is owed (or is permitted to draw) in connection therewith; and (f) expire not earlier than thirty (30) days following the expiration of the term of this Lease, provided however such Letter of Credit may expire one (1) year following date of issuance but in such case Tenant shall deliver a replacement Letter of Credit and subsequent replacement Letters

of Credit not less than thirty (30) days prior to the expiration of any existing Letter of Credit so that the original Letter of Credit or a replacement thereof (each of whose expiration date shall be not earlier than one year from issuance) shall be in full force and effect throughout the term of this Lease and for a period of at least ninety (90) days thereafter. Tenant shall maintain the Letter of Credit in the amount of the Security Deposit and shall deliver to Landlord any replacement Letter of Credit not less than thirty (30) days prior to the expiration of the then current Letter of Credit. Notwithstanding anything in this Lease to the contrary, any grace period or cure periods which are otherwise applicable under Section 8.1 hereof, shall not apply to any of the foregoing, and, specifically, if Tenant fails to comply with the requirements of subsection (f) above or if Tenant shall fail to maintain the Letter of Credit in the full amount of the Security Deposit after any draw thereon by Landlord, Landlord shall have the immediate right to draw upon the Letter of Credit in full and hold the proceeds thereof as a cash security deposit. Each Letter of Credit shall be issued by a commercial bank that has a credit rating with respect to certificates of deposit, short term deposits or commercial paper of at least P-2 (or equivalent) by Moody's Investor Service, Inc., or at least A-2 (or equivalent) by Standard & Poor's Corporation. If the issuer's credit rating is reduced below P-2 (or equivalent) by Moody's Investor Service, Inc., or at least A-2 (or equivalent) by Standard & Poor's Corporation, or if the financial condition of the issuer changes in any other materially adverse way, then Landlord shall have the right to require that Tenant obtain from a different issuer a substitute Letter of Credit that complies in all respects with the requirements of this Section, and Tenant's failure to obtain such substitute Letter of Credit within ten (10) days after Landlord's demand therefor (with no other notice, or grace or cure period being applicable thereto) shall entitle Landlord immediately to draw upon the existing Letter of Credit in full, without any further notice to Tenant. Landlord may use, apply or retain the proceeds of the Letter of Credit to the same extent that Landlord may use, apply or retain any cash security deposit, as set forth herein. If Landlord is entitled to draw on the Letter of Credit, Landlord may draw on the Letter of Credit, in whole or in part, at Landlord's election. If Landlord draws against the Letter of Credit, Tenant shall, within ten (10) days after notice from Landlord, provide Landlord with either an additional Letter of Credit in the amount so drawn or an amendment to the existing Letter of Credit restoring the amount thereof to the amount initially provided. Tenant hereby agrees to cooperate promptly, at its expense with Landlord to execute and deliver to Landlord any modifications, amendments and replacements of the Letter of Credit, as Landlord may reasonably request to carry out the terms and conditions hereof.

## Article 5

## Landlord's Covenants

5.1 Affirmative Covenants. Landlord shall, during the term of this Lease provide the following:

5.1.1 Heat and Air-Conditioning. Landlord shall provide and maintain air, chilled and hot water lines in accordance with the Work Matrix and with sufficient capacity to maintain the Premises at comfortable temperatures and levels of humidity comparable to those found in first class life science, research and development and general laboratory and office use in the Greater Boston/Cambridge/Somerville area, subject to all federal, state and municipal regulations. In particular, the temperature range (a) for the office portions of the Premises shall

be as follows: from 6:00 AM - 7:00 PM Monday through Friday, a temperature range of 68 to 72 degrees Fahrenheit, and (b) for the laboratory portions of the Premises shall be 68 to 72 degrees Fahrenheit twenty-four (24) hours per day, seven (7) days per week. The parties acknowledge
that individual occupants' comfort ranges may vary, and reasonable variations may be necessary for or desirable by Tenant, in which cases the parties shall reasonably confer to reconcile any differences. Landlord, as part of Tenant's Work, shall install all exhaust air ductwork, piping, terminal boxes, registers and controls to distribute all heat, ventilation and air conditioning ("HVAC") within the Premises. If the temperature otherwise maintained in any portion of the Premises by the HVAC system is affected as a result of (i) the type or quantity of any lights, machines or equipment used by Tenant in the Premises, (ii) the average occupancy of any portion of the Premises by more than one person per one hundred eighty-five (185) square feet of rentable area, (iii) an electrical load for lighting or power in excess of the limits specified in Subsection 6.2.4, or (iv) any partitioning or other improvements installed by Tenant, then at
Tenant's sole cost, Landlord may install any equipment, or modify any existing equipment Landlord deems necessary to restore the temperature balance. Tenant agrees to keep closed, when necessary, blinds or other window treatments which, because of the sun's position, must be closed to provide for the efficient operation of the air conditioning system, and Tenant agrees to cooperate with Landlord and to abide by the reasonable regulations and requirements which Landlord may prescribe for the proper functioning and protection of the HVAC system.
Landlord shall have no responsibility for providing any service from Separate HVAC Equipment, as defined in Subsection 6.1.3.

5.1.2 Cleaning; Water. Landlord shall provide cleaning, maintenance and landscaping to the common areas of the Building and Property (including snow removal to the extent necessary to maintain reasonable access to the Building) in accordance with standards generally prevailing throughout the term hereof in comparable office buildings in the greater Somerville area. Notwithstanding anything contained herein to the contrary, in no event shall Landlord's cleaning or janitorial obligations relate to or refer to any of the following:

(i) Any waste that is generated in the diagnosis, treatment, or immunization of human beings or animals, in research pertaining thereto, or in the production or testing of biologicals,

(ii) Any waste, device, instrument or item that comes in contact with bodily fluids, including, but not limited to, bandages, swabs, gauze, sponges, wraps, pads, paper, plastic, sutures, needles, scalpels, blades, or syringes,

(iii) Any medical device or paraphernalia that is utilized to treat any patient or other person for any medicinal, medical, diagnostic or therapeutic reason or purpose,

(iv) Any material of any type or nature whatsoever that is radioactive to any degree, whether as the result of its manufacture, use or application or any device, instrument or item that emits radiation,

(v) Any waste that is considered a regulated medical waste, including, but not limited to, bio-hazardous waste or infectious waste, under any applicable laws, or

(vi) Any device, instrument or item that has become infected, contaminated, diseased, or otherwise exposed to harmful, contagious, or communicable organisms, bacteria, or other life form.

Tenant and Landlord agree that the removal, disposal, or destruction of all items listed in the preceding paragraphs of this Subsection 5.1.2 (hereinafter "Excepted Waste") shall be exclusively the responsibility of Tenant under all circumstances, and their disposal shall not become the obligation of Landlord for any reason. All such disposals of Excepted Waste shall comply with all applicable laws and shall be accomplished at times, in a manner and in a path approved in writing and in advance by Landlord. Tenant agrees that Excepted Waste will be disposed of separately from any trash that is removed by Landlord. Tenant also agrees that Tenant will not mix or place Excepted Waste in regular trash containers. Tenant shall be permitted, subject to Landlord's review and approval, to install a two-hour rated waste storage area, such waste storage area to be no larger than 144 usable square feet, in the location shown on Exhibit L attached hereto. The parties agree that Tenant shall be liable in the event any harm or injury, of any type or nature whatsoever, is related to, incurred by, inflicted upon, or suffered by any individual including, but not limited to, Tenant, Landlord, or any of their respective agents, employees, guests, visitors, invitees or licensees, as the result of Tenant's or any of its partner's, subpartner's and their respective officer's, agent's, servant's, employee's, invitee's and independent contractor's (collectively, "Tenant Parties") failure to timely, thoroughly and completely dispose of Excepted Waste, the manner in which such disposal is accomplished, or coming into contact with, whether by touching, breathing, inhaling, or in any other manner ingesting or consuming such Excepted Waste, or by being exposed in any manner thereto and Tenant shall indemnify, defend, protect, and hold harmless Landlord and Landlord's Agents and their respective agents, employees and contractors, (collectively, "Landlord Parties") from and against any and all loss, cost, damage, expense and liability (including, without limitation, court costs and reasonable attorneys' fees) incurred in connection with or arising therefrom and save and hold other tenants, agents, employees, patients, visitors, invitees or licensees harmless against any damages, liability, claims, causes of action or judgments arising therefrom. Tenant shall be liable to and shall pay any injured party for all damages, costs or expenses, including attorney fees, arising out of any exposure, harm, injury, disease, contamination, or affliction suffered as the result of any Excepted Waste stored, generated, or disposed of by Tenant or in the Premises. Tenant shall provide to Landlord any written plan of Excepted Waste management Tenant prepares. Tenant shall contract with a reputable medical waste disposal company that shall be approved by Landlord and shall maintain all records regarding the disposal of Excepted Waste required by federal, state and local law or regulation and make such records available for Landlord review upon request.

5.1.3 Elevator, Lighting and Electricity. Landlord shall, as part of Operating Costs, furnish non-exclusive passenger elevator service from the lobby to the Premises with at least one (1) elevator available at all times; freight elevator service with at least one (1) elevator available at all times; purchase and install, at Tenant's expense, all building standard lamps, tubes, bulbs, starters and ballasts for lighting fixtures in the Premises; and provide lighting to

public and common areas of the Property. Landlord shall install and maintain lighting on the Land along walkways leading to nearby subway stations. In addition, Landlord shall use commercially reasonable efforts to coordinate with the City of Somerville to install, or cause to be installed, emergency "call boxes" on the Land if reasonably necessary, based on actual circumstances in the vicinity of the Land, for safety purposes.

5.1.4 Repairs. Except as otherwise expressly provided herein, Landlord shall, as part of Operating Costs (but subject to the limitations set forth therein), make such repairs and replacements to the roof, exterior walls, floor slabs and other structural components of the Building, and to the common areas and facilities of the Building (including any common plumbing, electrical and HVAC equipment, elevators and any other common equipment or systems in the Building) as may be necessary to keep them in good repair and condition consistent with first class life sciences, research and development office and laboratory facilities in the Greater Boston/Cambridge/Somerville Area (exclusive of equipment installed by Tenant and except for those repairs required to be made by Tenant pursuant to Subsection 6.1.3 hereof and repairs or replacements occasioned by any act or negligence of Tenant, its servants, agents, customers, contractors, employees, invitees, or licensees).

5.2 Interruption. Landlord shall have no responsibility or liability to Tenant for failure, interruption, inadequacy, defect or unavailability of any services, facilities, utilities, repairs or replacements or for any failure or inability to provide access or to perform any other obligation under this Lease caused by breakage, accident, fire, flood or other casualty, Force Majeure or due to any negligent act or omission of Tenant or Tenant's servants, agents, employees or licensees, and in no event shall Landlord be liable to Tenant for any indirect or consequential damages suffered by Tenant due to any such failure, interruption, inadequacy, defect or unavailability; and neither any failure or omission on the part of Landlord to furnish any of same for any of the reasons set forth in this paragraph nor any promulgation by any governmental authority affecting the Premises or its use thereof shall be construed as an eviction of Tenant, actual or constructive, nor entitle Tenant to an abatement of rent, nor render Landlord liable in damages, nor release Tenant from prompt fulfillment of any of its covenants under this Lease.

Landlord reserves the right to deny access to the Building and to interrupt the services of the HVAC, plumbing, electrical or other mechanical systems or facilities in the Building when necessary from time to time by reason of accident or emergency, or for repairs, alterations, replacements or improvements which in the reasonable judgment of Landlord are desirable or necessary, until such repairs, alterations, replacements or improvements shall have been completed. Landlord shall use reasonable efforts to minimize the duration of any such interruption and to schedule same outside of Normal Building Operating Hours, and Landlord shall give Tenant at least seven (7) Business Days' notice if service is to be interrupted, except in cases of emergency, in which case Landlord shall give Tenant as much notice as possible under the circumstances.

If due to Landlord's default or the negligent act or omission of Landlord or Landlord's servants, agents, employees or contractors (i) an Essential Service (as defined below) is not provided to the Premises and Tenant is unable to use the Premises or any portion thereof are unusable by Tenant for a period of more than three (3) consecutive Business Days following the

date on which Tenant gives notice thereof, complying with the last sentence of this paragraph, to Landlord, and (ii) Tenant shall, concurrently with the giving of such notice, discontinue use of the Premises or such portion thereof as result (other than for sporadic purposes such as salvage, security or retrieval of property) (the conditions in clauses (i) and (ii) being the "Abatement Conditions"), then as Tenant's sole remedy the Annual Fixed Rent and Additional Rent on account of Taxes and Operating Costs shall be equitably abated for such portion of the Premises rendered unusable for the period commencing on the expiration of such three (3) Business Day period and ending on the first full Business Day that the Essential Service is provided to the Premises and the Premises (or such portion) is rendered usable. "Essential Services" as used in this paragraph shall be HVAC, electricity, gas, sewer, water and the Laboratory Systems. Any notice from Tenant pursuant to the first sentence of this paragraph shall expressly state that the failure of Landlord to cure any claimed default timely shall give rise to Tenant's rights of rent abatement. If Tenant is unable to use the entire laboratory portion of the Premises due to Abatement Conditions that continue for more than two (2) consecutive months and as a result of such Abatement Conditions Tenant discontinues use of the entire laboratory portion of the Premises for more than two (2) consecutive months, Tenant shall be entitled, in addition to the abatement set forth above, to a credit against Annual Fixed Rent and Additional Rent on account of Taxes and Operating Costs that would otherwise be due for each day after such two (2) consecutive month abatement period until such time as the Essential Service is provided to the Premises and the Premises is rendered usable, which credit shall be applied against Annual Fixed Rent and Additional Rent on account of Taxes and Operating Costs first coming due hereunder. Landlord agrees to use reasonable efforts to minimize the duration of any Abatement Conditions and to keep Tenant reasonably informed as to the status of the restoration of Essential Services.

5.3 Outside Services. In the event Tenant wishes to obtain services or to hire vendors relating to the Premises (as opposed to the operation of Tenant's business), Tenant shall first obtain the prior approval of Landlord for the installation and/or utilization of such services or vendors, which approval shall not be unreasonably withheld, conditioned or delayed. Such services shall include, but shall not be limited to, utility providers and moving services, but this Section 5.3 shall not apply to mail or package delivery services, caterers, persons or firms servicing or installing Tenant's business or laboratory equipment at the Premises, facility management services, security services, cleaning services (provided any cleaning providers satisfy Landlord's reasonable insurance requirements) or to the vendors of supplies, materials or other items used by Tenant in the ordinary conduct of its business.

5.4 Access to Building. During Normal Building Operating Hours, the Building shall, subject to the provisions of Section 5.2, be open and access to the Premises shall be freely available, subject to the Rules and Regulations as more particularly set forth in Subsection 6.1.9. During periods other than Normal Building Operating Hours, Tenant shall have access to the Premises, but such access shall also be subject to the Rules and Regulations. Tenant acknowledges that Tenant is responsible for providing security to the Premises following Tenant's entry onto the Premises for any reason and for its own personnel whenever located therein.

Tenant shall have the right to provide, install, repair, replace, and remove its own security system providing access to and within the Premises, provided that Tenant shall provide Landlord with the proper access codes or keys necessary for Landlord to obtain access to the Premises.

This shall include the right to install, in a good and workmanlike fashion and in compliance with applicable laws, codes and regulations, system components of Tenant's choosing that include but are not limited to security cameras within the Premises, televisions, monitors and other electronic monitoring devices within the Premises; electronic door strikes; door contacts; exit sensors; card readers (which may be mounted immediately outside the Premises in common areas, if any); motion detectors; glass break detectors, and other similar security systems and/or methods which will protect the Premises to meet Tenant's corporate security standards. Tenant shall provide Landlord with advance written notice of any such planned security-related installation, repair, replacement, and removal; provided, however, Landlord acknowledges that it shall not have access to certain areas within the Premises. Tenant shall be responsible for the reasonable restoration costs once the security system(s) have been removed. To the extent that Tenant's security systems require integration with Landlord's security systems, Landlord shall have the right to reasonably review and approve Tenant's security systems integration plan. To the extent that Tenant's security systems includes the installation of cameras located outside of the Premises, Landlord shall have the right to reasonably review and approve the area of focus of such cameras. To the extent that Tenant's security systems affect the structure or aesthetics of the Building outside of the Premises or inside the Premises but visible from outside of the Premises, Tenant's installation shall be treated as an alteration and shall be subject to Subsection 6.2.5 below.

5.5 Parking. During the term of this Lease, and subject in all events to the Mobility Management Plan or similar requirements applicable to the Property, Tenant's employees shall have the right to enter into contracts for up to 1.25 parking spaces per 1,000 square feet of Premises Rentable Area (i.e., fifty-three (53), as of the Date of this Lease) of the parking spaces in the parking garage located on the Property (the "Parking Facility") on an unreserved, "first come-first served" basis at the Monthly Rate (as defined below), from time to time, per space per month, plus tax, without set-off or deduction. Landlord shall arrange for the Parking Facility to be operated by a third party (an "Operator") which may exercise any or all of the rights of Landlord under this Section 5.5, as determined by Landlord and all parking fees and charges shall be paid directly to the Operator.

Tenant's employees to whom such right is granted shall enter into separate contracts with the Operator for the use of such parking spaces and each such employee shall pay the Monthly Rate for each such parking space directly to the Operator. If Tenant's employees do not enter into contracts for all of the parking spaces to which it is entitled hereunder within thirty (30) days after the Commencement Date, or shall cancel any such contracts during the term and not enter into a replacement contract within thirty (30) days, the Operator shall be free to enter into contracts with other parties for such spaces; provided, however, that in the event that, at any time during the term of this Lease, Tenant's allocated number of parking spaces has been reduced below the allocated number of parking spaces to which Tenant is initially entitled hereunder pursuant to the foregoing provisions of this Section ("Tenant's Initial Parking Allocation"), and Tenant thereafter determines that Tenant desires to use additional parking spaces, Tenant shall have the right from time to time to request that Landlord provide additional parking spaces to Tenant (but not a number of parking spaces that would cause the number of parking spaces which Tenant has the right to use hereunder to exceed Tenant's Initial Parking Allocation), and, in such event Landlord shall, within thirty (30) days following receipt of Tenant's request, make available to Tenant such requested number of parking spaces to Tenant for its use hereunder (on

the terms set forth in this Section) to the extent that parking spaces in the Parking Facility remain available for use by Tenant after meeting Landlord's current and projected parking requirements for the Property as determined by Landlord in good faith.

Subject to the MMP, Tenant and its employees shall have the right to lease additional parking spaces, in addition to Tenant's Initial Parking Allocation, from time to time to the extent that parking spaces in the Parking Facility remain available for use by Tenant after meeting Landlord's current parking requirements for the Property as determined by Landlord in good faith.

Landlord shall have the right (but not the obligation), to adjust the amount Tenant is charged each month for each parking space to equal the commercially reasonable rate from time to time designated by Landlord as standard for the Parking Facility (the "Monthly Rate"); provided, however, in no event shall Tenant pay a higher Monthly Rate than other tenants or occupants of the Building. Tenant, its employees and invitees shall use the Parking Facility for the parking of passenger vehicles only and shall not allow any of its vehicles, or any vehicles on the Parking Facility through Tenant, to be left in the Parking Facility overnight. Landlord reserves the right to (a) implement and modify systems to regulate access to and use of the Parking Facility, (b) designate and redesignate reserved and unreserved parking areas within the Parking Facility (for some or all tenants); provided, however, if any tenant or occupant of the Building has the right to reserved parking spaces, Tenant shall have the right to a proportionate number of reserved parking spaces, (c) change entrances or exits and alter traffic flow within the Parking Facility, and (d) modify the Parking Facility to any extent. Landlord further reserves the right to close the Parking Facility or portions thereof temporarily to the extent necessary for maintenance and repairs, provided that, except in the case of emergency Landlord shall provide Tenant with not less than fifteen (15) days' prior notice of any such closure. Tenant acknowledges that Landlord is not required to provide any security or security services for any of the Parking Facility, provided that Landlord shall provide reasonable security systems, services and/or protocols as Landlord deems appropriate, in its discretion, to the Parking Facility, the cost of which shall be included as an Operating Cost. Tenant shall indemnify and agrees to defend and hold Landlord and the Operator harmless from and against all claims, loss, cost, or damage arising out of the use by Tenant and its employees and invitees of the Parking Facility, except to the extent caused by negligence or willful misconduct of Landlord or Landlord's agent or employees or the Operator. Tenant shall, and shall use reasonable efforts to cause its employees to, comply with all reasonable rules and regulations pertaining to the Parking Facility, as the same may be established amended, revised or supplemented by Landlord or the Operator.

5.6 Landlord's Hazardous Waste Representation. Landlord represents, covenants and agrees that Landlord shall comply with Environmental Laws (as defined in Subsection 6.2.8) at the Property. Landlord further warrants and represents that to the best of Landlord's knowledge, on the Commencement Date, the Premises and the Property will be in compliance with applicable Environmental Laws relating to the use, treatment, disposal, storage, control, removal or cleanup of Hazardous Materials. If any Hazardous Materials (as defined in Subsection 6.2.8) are discovered at the Property in violation of Environmental Laws, then so long as the condition requiring removal or remediation of Hazardous Materials is not caused or exacerbated by Tenant or any party for whom Tenant is responsible, Landlord shall, in a manner that complies with all applicable Environmental Laws, perform or cause others to perform all remediation and cleanup

of the Premises, the Building and land necessary to cause the Property to comply in all material respects with Environmental Laws. Landlord shall indemnify and defend Tenant from any liability for fines or penalties arising from a breach by Landlord of the forgoing representations and agreements of Landlord and from any liability for costs of investigating or monitoring of site conditions, repair cleanup, containment, remediation, removal or restoration work or detoxification of the Property pursuant to this paragraph. Landlord agrees that Operating Costs shall not include the cost of investigating or monitoring of site conditions, repair cleanup, containment, remediation, removal or restoration work or detoxification of the Property in connection with any Hazardous Materials on or under the Property as of the Date of this Lease or which migrates onto the Property after the Date of this Lease from abutting property.

5.7 Indemnification. Subject to Section 10.4 and Section 10.5, and to the extent not subject to the provisions of Subsection 4.4.4, Landlord shall neither hold, nor attempt to hold, Tenant or its employees or Tenant's agents or their employees liable for, and Landlord shall indemnify and hold harmless Tenant, its employees and Tenants agents and their employees from and against, any and all demands, claims, causes of action, fines, penalties, damage,
liabilities, judgments and expenses (including, without limitation, reasonable attorneys' fees): (i) asserted by or on behalf of any third party and arising from any negligent acts, omissions or negligence of Landlord, its contractors, agents, employees; and (ii) any breach, violation or nonperformance by Landlord of any term, covenant or provision of this Lease or any law, ordinance or governmental requirement of any kind. If any action or proceeding is brought
against Tenant or its employees or Tenant's agents or their employees by reason of any such claim, Landlord, upon notice from Tenant, shall defend the same, at Landlord's expense, with counsel reasonably satisfactory to Tenant. Notwithstanding the foregoing in no event shall this
Section require Landlord to indemnify or defend Tenant, its employees and Tenants agents and their employees against any demands, claims, causes of action, fines, penalties, damage, liabilities, judgments and expenses to the extent arising out of the negligence or willful misconduct of Tenant or its employees or agents or their employees.

## Article 6

## Tenant's Additional Covenants

6.1 Affirmative Covenants. Tenant shall do the following:

6.1.1 Perform Obligations. Tenant shall perform promptly all of the obligations of Tenant set forth in this Lease; and pay when due the Annual Fixed Rent and Additional Rent and all other amounts which by the terms of this Lease are to be paid by Tenant.

6.1.2 Use. Tenant shall, during the term of this Lease, use the Premises only for the Permitted Uses and from time to time, procure and maintain all licenses and permits necessary therefor and for any other use or activity conducted at the Premises, at Tenant's sole expense. Nothing contained in the definition of "Permitted Use" shall prohibit, restrict or limit the access, use and temporary occupancy of the Premises by a government, local, state or federal agency as required by such agency in connection with the ordinary course of Tenant's business. Landlord and Tenant shall, from time to time, provide to the other the name and contact information for a representative of such party with whom issues relating to sustainability and

energy use may be communicated. Such issues may include, but not be limited to, retrofitting projects, building issues, energy efficiency upgrades and data access. Tenant acknowledges that this Lease is subject to that certain Notice of Activity and Use Limitation dated September 12, 2019, and recorded with the Middlesex (Southern District) Registry of Deeds at Book 73303, Page 185, and the Mobility Management Plan, and Tenant shall comply with the terms and requirements thereof.

In addition, Tenant acknowledges that this Lease is subject to the Mobility Management Plan ("MMP") for the Property that was issued by the City of Somerville on May 20, 2021, a copy of which is attached hereto as Exhibit H, as the same may be amended, modified or supplemented from time to time. Tenant acknowledges that Tenant, at its sole cost and expense, shall comply with the tenant requirements in the MMP including, without limitation, the preparation and submission to the City of Somerville of a Mobility Management Plan for Tenant's employees and the designation of a liaison to work with employees as a transportation coordinator. Additional requirements may include (i) offering employees the right to contract for the parking spaces to which Landlord is entitled as further set forth in Section 5.5 below, (ii) subsidizing mass transit monthly passes for employees, (iii) allowing employees to use pre-tax funds for Commuter Choice programs, (iv) offering an emergency ride home program, and (v) encouraging employees to make use of alternate modes of transportation. Tenant, at its sole cost and expense and at Landlord's request, shall also comply with the reporting requirements set forth in the MMP that are applicable to tenants in the Building.

6.1.3 Repair and Maintenance. Tenant shall, during the term of this Lease, maintain the non-structural (unless installed by Tenant), interior portions of the Premises in neat and clean order and condition and perform all repairs to the Premises and all fixtures, systems, and equipment therein (including Tenant's equipment and other personal property and any HVAC Equipment serving all or any portion of the Premises to the exclusion of any other space in the Building ("Separate HVAC Equipment")) as are necessary to keep them in good and clean working order, appearance and condition, reasonable use and wear thereof and damage by fire or by unavoidable casualty only excepted and shall replace any damaged or broken glass in windows and doors of the Premises (except glass in the exterior walls of the Building) with glass of the same quality as that damaged or broken. Tenant shall contract separately for janitorial services for the Premises with Landlord's janitorial services provider or another janitorial services provider reasonably acceptable to Landlord and Tenant shall cause the Premises to be
cleaned in accordance standards at least equal to Landlord's janitorial standards for leased space in the Building. Tenant shall dispose of all trash and rubbish in such manner as Landlord reasonably directs and shall comply with any reasonable recycling programs established by Landlord for the Building.

6.1.4 Compliance with Law. Tenant shall, during the term of this Lease, make all repairs, alterations, additions or replacements to the Premises required by any law or ordinance or any order or regulation of any public authority; keep the Premises safe and equipped with all safety appliances so required; and comply with, and perform all repairs, alterations, additions or replacements required by, 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 other portions of the Property and arising out of any use being conducted in or on the Premises or arising out of any work performed by Tenant.

6.1.5 Indemnification. Tenant shall neither hold, nor attempt to hold, Landlord or its employees or Landlord's agents or their employees liable for, and Tenant shall indemnify and hold harmless Landlord, its employees and Landlord's agents and their employees from and against, any and all demands, claims, causes of action, fines, penalties, damage, liabilities, judgments and expenses (including, without limitation, reasonable attorneys' fees) incurred in connection with or arising from: (i) the use or occupancy or manner of use or occupancy of the Premises by Tenant or any person claiming under Tenant except due to Landlord's or its agents', employees' or contractors' negligent act or omission; (ii) any matter occurring on the Premises during the term; (iii) the negligent acts or omissions of Tenant or its contractors, agents, employees or invitees; (iv) any breach, violation or nonperformance by Tenant of any term, covenant or provision of this Lease or any law, ordinance or governmental requirement of any kind; and (v) claims of brokers or other persons for commissions or other compensation arising out of any actual or proposed sublease of any portion of the Premises or assignment of Tenant's interest under this Lease, or Landlord's denial of consent thereto. If any action or proceeding is brought against Landlord or its employees or Landlord's agents or their employees by reason of any such claim, Tenant, upon notice from Landlord, shall defend the same, at Tenant's expense, with counsel reasonably satisfactory to Landlord. Notwithstanding the foregoing in no event shall this Subsection 6.1.5 require Tenant to indemnify or defend Landlord or its employees or Landlord's agents or their employees against any loss, cost, damage, liability, claim, or expense to the extent arising out of the gross negligence or willful misconduct of Landlord or its employees or Landlord's agents or their employees.

6.1.6 Landlord's Right to Enter. Tenant shall, during the term of this Lease, permit Landlord and its agents and invitees to enter the Premises at reasonable times and upon not less than one (1) Business Day prior notice (except in the case of an emergency), which notice may be email, and to examine the Premises and to show the Premises to prospective lenders, partners and purchasers and others having a bonafide interest in the Premises, and to make such repairs, alterations and improvements and to perform such testing and investigation as Landlord shall reasonably determine to make or perform, and, during the last twelve (12) months of the term, show the Premises to prospective tenants; provided in all such circumstances Landlord shall use commercially reasonable efforts minimize interference with Tenant's use of the Premises. In case of any such entry by Landlord Tenant shall have the right to have a representative accompany Landlord, its agents, and invitees when accessing the Premises.
Tenant may designate areas of the Premises as "Secured Areas" as Tenant may, in its sole discretion determine, for the purpose of securing certain property or confidential information or which are used for laboratory purposes. In connection with the foregoing, Landlord shall not enter such Secured Areas except in the event of an emergency.

6.1.7 Personal Property at Tenant's Risk. Tenant shall, during the term of this Lease keep, at the sole risk and hazard of Tenant, all of the furnishings, fixtures, equipment, effects and property of every kind, nature and description of Tenant and of all persons claiming by, through or under Tenant which may be on the Property.

6.1.8 Yield Up. Tenant shall, at the expiration or earlier termination of the term of this Lease, or upon any earlier reentry or retaking of possession of the Premises by Landlord and/or termination of Tenant's right of possession and/or occupancy of the Premises, as applicable, surrender all keys to the Premises; remove all of its trade fixtures and personal

property in the Premises; remove such Alterations, signs and improvements made (or if applicable, restore any items removed) by or at Tenant's request, as set forth in the following paragraph; repair all damage caused by such removal; repair all damage caused by such removal; and vacate and yield up the Premises broom clean and in the same good order and repair in which Tenant is obligated to keep and maintain the Premises by the provisions of this Lease.
Tenant shall not be required to remove Landlord's Work or Tenant's Work. If the term of the Lease is extended beyond the Original Term, Landlord shall have the right to require Tenant to properly cap or seal its wiring and cabling (wherever located) at each end, properly label such wiring and cabling for future use, and surrender such wiring and cabling in a good and safe condition upon the expiration or earlier termination of the term. Any property not so removed shall be deemed abandoned and may be removed and disposed of by Landlord in such manner as Landlord shall determine and Tenant shall pay Landlord the entire reasonable, out-of-pocket cost and expense incurred by it in effecting such removal and disposition and in making any incidental repairs and replacements to the Premises required due to such removal.

Notwithstanding the preceding provisions of this Subsection 6.1.9, except for cabling as provided above, Tenant shall not be required to remove alterations made by it in the Premises if
(i) Tenant's request for Landlord's consent to make such alterations contains a statement in capital letters notifying Landlord that Landlord shall have waived its right to require removal of such alterations at the end of the term unless Landlord's consent to such alterations requires, as a condition to Landlord's consent, that Tenant is required to remove the alteration at the end of the term, and (ii) Landlord does not so notify Tenant that removal shall be required.

6.1.9 Rules and Regulations. Tenant shall, during the term of this Lease, observe and abide by the Rules and Regulations of the Building set forth as Exhibit B, as the same may from time to time be amended, revised or supplemented (the "Rules and Regulations"), provided that such amendments, revisions or supplements shall not materially change the obligations of Landlord or Tenant as set forth in this Lease as of the Date of this Lease. Tenant shall further be responsible for compliance with the Rules and Regulations by the employees, servants, agents and visitors of Tenant. The failure of Landlord to enforce any of the Rules and Regulations against Tenant, or against any other tenant or occupant of the Building, shall not be deemed to be a waiver of such Rules and Regulations. In the event of a conflict between the express terms of this Lease and any requirement of the Rules and Regulations, the terms of this Lease shall control. Landlord agrees that it shall apply the Rules and Regulations in a nondiscriminatory manner, but Landlord may waive Rules and Regulations with respect to particular tenants when Landlord shall have a good faith basis to do so.

6.1.10 Estoppel Certificate. Tenant shall, within fifteen (15) days' following written request by Landlord, execute, acknowledge and deliver to Landlord a statement in form satisfactory to Landlord in writing certifying that this Lease is unmodified and in full force and effect and that Tenant has no defenses, offsets or counterclaims against its obligations to pay the Annual Fixed Rent and Additional Rent and any other charges and to perform its other covenants under this Lease (or, if there have been any modifications, that this Lease is in full force and effect as modified and stating the modifications and, if there are any defenses, offsets or counterclaims, setting them forth in reasonable detail), the dates to which the Annual Fixed Rent and Additional Rent and other charges have been paid, and any other matter pertaining to this Lease. Any such statement delivered pursuant to this Subsection 6.1.11 may be relied upon by

any prospective purchaser or mortgagee of the Property, or any prospective assignee of such mortgage.

6.1.11 Landlord's Expenses For Consents. Tenant shall reimburse Landlord, as Additional Rent, promptly on demand for all reasonable, out-of-pocket legal, engineering and other professional services expenses incurred by Landlord in connection with all requests by Tenant for consent or approval hereunder; provided, however, that Landlord shall use reasonable efforts to minimize expenses for which Tenant shall be liable under this Subsection 6.1.11, including by conducting such reviews itself to the extent reasonably feasible; and provided further that such reimbursement obligation shall not exceed $2,500.00 in connection with any request for approval pursuant to Subsection 6.2.1 where Tenant, any assignee and/or any subtenant, as the case may be, agree to execute Landlord's standard form of consent.

6.1.12 Financial Information. Tenant shall, from and after the Date of this Lease and thereafter throughout the term of this Lease, provide Landlord (but not more frequently than once in any 12-month period except in connection any financing of the Property or of Landlord and in connection with any sale or transfer of the Property) with Tenant's most recently completed financial statements (audited if available). Landlord and its affiliates and investors shall keep such financial statements confidential, provided that Landlord shall be permitted to deliver such financial statements to a lender, purchaser or lessor or a prospective lender or purchaser, so long as Landlord first advises the recipient of the confidential nature of such statements, or to the extent required by Law. Notwithstanding the foregoing, if Tenant's financial statements or reasonably equivalent information are publicly disclosed and readily available, Tenant shall have no obligation to deliver any financial statements to Landlord.

6.2 Negative Covenants. Tenant shall not do the following.

6.2.1 Assignment and Subletting. Tenant shall not assign, mortgage, pledge, hypothecate, encumber or otherwise transfer this Lease or any interest herein or sublease (which term shall be deemed to include the granting of concessions and licenses and the like) all or any part of the Premises or suffer or permit this Lease or the leasehold estate hereby created or any other rights arising under this Lease to be assigned, transferred, mortgaged, pledged, hypothecated or encumbered, in whole or in part, whether voluntarily, involuntarily or by operation of law, or permit the use or occupancy of the Premises by anyone other than Tenant, or the Premises to be offered or advertised for assignment or subletting, without first obtaining Landlord's prior written consent, which shall not be unreasonably withheld, conditioned or delayed as set forth herein, except as hereinafter provided except as hereinafter provided.

Notwithstanding the foregoing, Tenant may, without the need for Landlord's consent, assign its interest in this Lease (a "Permitted Assignment") to (i) any entity which shall be a successor to Tenant either by merger or consolidation (a "Merger") or to a purchaser of all or substantially all of Tenant's assets in either case provided the successor or purchaser shall have a tangible net worth, after giving effect to the transaction, of not less than $500,000,000.00 (the "Required Net Worth") or (ii) any entity (an "Affiliate") which is a direct or indirect subsidiary or parent (or a direct or indirect subsidiary of a parent) of the named Tenant set forth in Section 1.1, in either case of (i) or (ii) provided that (I) the principal purpose of such assignment is not the acquisition of Tenant's interest in this Lease (except if such assignment is made for a valid

intracorporate business purpose to an Affiliate) and is not made to circumvent the provisions of this Subsection 6.2.1. In connection with a Permitted Assignment pursuant to clause (ii) above, Tenant shall deliver to Landlord a copy of an assignment document which evidences the assignment to Tenant's Affiliate and the Affiliate's assumption of Tenant's obligations under this Lease. Tenant shall also be permitted, without the need for Landlord's consent, to enter into any sublease (a "Permitted Sublease") with any Affiliate provided that such sublease shall expire upon any event pursuant to which the sublessee thereunder shall cease to be an Affiliate. Any assignment to an Affiliate shall provide that it may, at Landlord's election, be terminated and deemed void if during the term of this Lease such assignee or any successor to the interest of Tenant hereunder shall cease to be an Affiliate. Tenant shall give Landlord notice of any Permitted Assignment or Permitted Sublease not later than ten (10) days after the date thereof and until Tenant shall have given Landlord such notice, Landlord shall have no obligation to any such subtenant nor shall any such assignee have any rights under this Lease.

In the event that Tenant shall intend to enter into any sublease or assignment other than a Permitted Sublease or Permitted Assignment, Tenant shall, not later than thirty (30) days prior to the proposed commencement of such sublease or assignment, give Landlord notice of such intent, identifying the proposed subtenant or assignee, all of the terms and conditions of the proposed sublease or assignment and such information as Landlord may reasonably request regarding the financial condition and identity of the proposed subtenant or assignee.

Landlord shall not unreasonably condition or withhold its consent to any sublease or assignment, provided that, in addition to any other grounds for withholding of consent, Landlord may withhold its consent if in Landlord's good faith judgment: (i) the proposed assignee or subtenant does not have a financial condition reasonably acceptable to Landlord; provided, however, that the financial condition may only be considered in connection with an assignment of this Lease following which Ultragenyx Pharmaceutical Inc. shall be dissolved or an assignment made in connection with Tenant's sale or other transfer of all or substantially all of its assets and which is not a Permitted Assignment; (ii) the business and operations of the proposed assignee or subtenant are not of reasonably comparable quality to the business and operations being conducted by the majority of other tenants in the Building; (iii) the proposed assignee or subtenant is a business competitor of Landlord or is an affiliate of a business competitor of Landlord; (iv) the identity of the proposed assignee or subtenant is, or the intended use of any part of the Premises, would be, in Landlord's reasonable determination, inconsistent with first-class office and laboratory space or in violation of any exclusivity provisions granted to other tenants in the Building of which Landlord has given written notice to Tenant or any covenants, conditions or restrictions binding on Landlord or applicable to the Property; (v) at the time of the proposed assignment or subleasing Landlord is able to meet the space requirements of Tenant's proposed assignee or subtenant by leasing available space in the Building to such person or entity on substantially the same terms and conditions as the proposed sublease and either (a) the proposed assignee or subtenant is a tenant or other occupant of the Building, or (b) the proposed assignee or subtenant is an entity, or is affiliated with any entity, which shall have entered into negotiation with Landlord for space in the Building within the preceding six (6) months; or (vi) any such sublease shall result in the Premises being occupied by more than four (4) parties (including Tenant but excluding any occupants or uses under a Shared Space Arrangement) at any one time, which such limitation shall increase on a proportional basis with any increases to the Premises.

If this Lease is assigned or if the Premises or any part thereof are sublet (or occupied by any party other than Tenant and its employees) Landlord may collect the rents from such assignee, subtenant or occupant, as the case may be, and apply the net amount collected to the Annual Fixed Rent and Additional Rent herein reserved, but no such collection shall be deemed a waiver of the provisions set forth in the first paragraph of this Subsection 6.2.1, the acceptance by Landlord of such assignee, subtenant or occupant, as the case may be, as a tenant, or a release of Tenant from the future performance by Tenant of its covenants, agreements or obligations contained in this Lease. All assignees shall have all of the rights, options and privileges of Tenant under the Lease. All assignees and subtenants shall have the appurtenant rights of Tenant under the Lease, including parking, use of the common areas and Building directory signage.

Any sublease of all or any portion of the Premises shall provide that it is subject and subordinate to this Lease and to the matters to which this Lease is or shall be subject or subordinate, that other than the payment of Annual Fixed Rent and Additional Rent due pursuant to Sections 4.1, 4.2.1 and 4.2.2 or any obligation relating solely to those portions of the Premises which are not part of the subleased premises, the subtenant shall comply with and be bound by all of the obligations of Tenant hereunder that are applicable to the portions of the Premises which are part of the subleased premises, that unless Landlord waives such prohibition, the subtenant may not enter into any sub-sublease, sublease assignment, license or any other agreement granting any right of occupancy of any portion of the subleased premises; and that Landlord shall be an express beneficiary of any such obligations, and that in the event of termination of this Lease or reentry or dispossession of Tenant by Landlord under this Lease, Landlord may, at its option, take over all of the right, title and interest of Tenant, as sublessor under such sublease, and such subtenant shall, at Landlord's option, attorn to Landlord pursuant to the then executory provisions of such sublease, except that neither Landlord nor any mortgagee of the Property, as holder of a mortgage or as Landlord under this Lease if such mortgagee succeeds to that position, shall (a) be liable for any act or omission of Tenant under such sublease, (b) be subject to any credit, counterclaim, offset or defense which theretofore accrued to such subtenant against Tenant, or (c) be bound by any previous modification of such sublease unless consented to by Landlord and such mortgagee or by any previous prepayment of more than one (1) month's rent, (d) be bound by any covenant of Tenant to undertake or complete any construction of the Premises or any portion thereof, (e) be required to account for any security deposit of the subtenant other than any security deposit actually received by Landlord, (f) be bound by any obligation to make any payment to such subtenant or grant any credits unless specifically agreed to by Landlord and such mortgagee, (g) be responsible for any monies owing by Tenant to the credit of subtenant or (h) be required to remove any person occupying the Premises or any part thereof; and such sublease shall provide that the subtenant thereunder shall, at the request of Landlord, execute a suitable instrument in confirmation of such agreement to attorn. Landlord shall deliver to Tenant written notice of its approval or disapproval of any proposed sublease or assignment, which such notice shall include a reasonable detailed explanation of any disapproval, within ten (10) Business Days after Tenant's written request of Landlord's approval, subject to extension for review by Landlord's lender, if required, Landlord agreeing to use reasonable efforts to cause the Landlord's lender to respond in as timely a manner as possible. The provisions of this paragraph shall not be deemed a waiver of the provisions set forth in the first paragraph of this Subsection 6.2.1 and any breach of any obligation of any subtenant of Tenant shall be attributable to Tenant and constitute a breach of this Lease by Tenant.

No subletting or assignment shall in any way impair the continuing primary liability of the Tenant named in Section 1.1, and any immediate or remote successor in interest, and no consent to any subletting or assignment in a particular instance shall be deemed to be a waiver of the obligation to obtain the Landlord's written approval in the case of any other subletting or assignment. The joint and several liability of Tenant named herein and any immediate and remote successor in interest (by assignment or otherwise) for the payment of Annual Fixed Rent and Additional Rent, and the timely performance of all non-monetary obligations on Tenant's part to be performed or observed, shall not in any way be discharged, released or impaired by any (a) agreement which modifies any of the rights or obligations of the parties under this Lease,
(b) stipulation which extends the time within which an obligation under this Lease is to be performed, (c) waiver of the performance of an obligation required under this Lease, or (d) failure to enforce any of the obligations set forth in this Lease. No assignment, subletting or occupancy shall affect the Permitted Uses. Any subletting, assignment or other transfer of Tenant's interest in this Lease in contravention of this Subsection 6.2.1 shall be voidable at
Landlord's option. Tenant shall not occupy any space in the Building (by assignment, sublease or otherwise) other than the Premises.

If the rent and other sums (including, without limitation, all monetary payments plus the reasonable value of any services performed or any other thing of value given by any assignee or subtenant in consideration of such assignment or sublease), either initially or over the term of any assignment or sublease (other than a Permitted Assignment or Permitted Sublease), payable by such assignee or subtenant shall exceed the Annual Fixed Rent plus Additional Rent called for hereunder (or in the case of a sublease of a portion of the Premises, shall exceed the Annual Fixed Rent plus Additional Rent attributable to the space so sublet), Tenant shall pay fifty percent (50%) of such excess to Landlord, as Additional Rent, payable monthly at the time for payment of Annual Fixed Rent, provided that in computing the amount of any such excess the amortized portion of the following "Transfer Expenses" paid by Tenant in connection with such assignment or sublease may first be deducted from the monthly amount of any such excess: (i) the cost of alterations or improvements made by Tenant to the Premises in order to consummate an assignment or to the portion of Premises that is subleased in order to consummate a sublease,
(ii) reasonable brokerage commissions or fees, and (iii) reasonable attorney's fees. Any such Transfer Expenses shall be amortized in equal monthly installments over the term of the assignment or sublease and shall be verified by Tenant by written documentation reasonably satisfactory to Landlord within sixty (60) days after the date of delivery of possession to the assignee or sublessee. Nothing in this paragraph shall be deemed to abrogate the provisions of
this Subsection 6.2.1 and Landlord's acceptance of any sums pursuant to this paragraph shall not be deemed a granting of consent to any assignment of the Lease or sublease of all or any portion of the Premises.

Notwithstanding anything to the contrary contained in this Lease, Tenant may from time to time enter into license agreements (each, a "Shared Space Arrangement") with Tenant's agents, contractors, consultants or affiliates pursuant to which such agents, contractors, consultants or affiliates (including, without limitation, special purpose vehicles and collaboration with university and/or hospital researchers, regardless of whether or not the collaboration is funded by standalone investors) may occupy up to twenty-five percent (25%) of the Premises Rentable Area as "Shared Space Area", and such license agreements shall not require Landlord's consent under this Subsection 6.2.1; provided, however, that prior to the effective date of each

such Shared Space Arrangement, Tenant and each licensee shall be required to execute Landlord's reasonable form of acknowledgment, attached hereto as Exhibit I, pursuant to which Tenant and the licensee acknowledge and agree that: (i) the terms of the Shared Space Arrangement are subject and subordinate to the terms of this Lease, (ii) if this Lease terminates, then the Shared Space Arrangement shall terminate concurrently therewith, and (iii) the waivers and releases between Landlord and Tenant shall also apply as between Landlord and licensee.
Tenant shall be fully responsible for the conduct of such entities within the Shared Space Area, and Tenant's indemnification obligations set forth in this Lease shall apply with respect to the conduct of such parties within the Shared Space Area. The portion of the Premises subject to any such Shared Space Arrangements shall not exceed a total of twenty-five percent (25%) of the Premises Rentable Area.

6.2.2 Nuisance. Tenant shall not injure, deface or otherwise harm the Premises; nor commit any nuisance; nor permit in the Premises any vending machine (except such as is used for the sale of merchandise to employees of Tenant) or inflammable fluids or chemicals (except such as are customarily used in connection with standard office equipment or Tenant's Permitted Uses); nor permit any cooking to such extent as requires special exhaust venting; nor permit the emission of any noxious odor; nor make, allow or suffer any waste; nor make any use of the Premises which is improper, offensive or contrary to any law or ordinance or which will invalidate or increase the premiums for any of Landlord's insurance or which is liable to render necessary any alteration or addition to the Building; nor conduct any auction, fire, "going out of business" or bankruptcy sales.

6.2.3 Floor Load; Heavy Equipment. Tenant shall not place a load upon any floor of the Premises exceeding the lesser of the floor load capacity which such floor was designed to carry (being 100 pounds per square foot live load) or which is allowed by law. Landlord reserves the right to prescribe the weight and position of all heavy business machines and equipment, including safes, which shall be placed so as to distribute the weight. Business machines and mechanical equipment which cause vibration or noise shall be placed and maintained by Tenant at Tenant's expense in settings sufficient to absorb and prevent vibration, noise and annoyance. Tenant shall not move any safe, heavy machinery, heavy equipment, freight, construction materials or fixtures into or out of the Premises without Landlord's prior consent which consent may include a requirement to provide insurance naming Landlord, and the holder of any mortgage affecting the Property, as additional insureds, with such coverage and in such amount as Landlord reasonably requires. If any such safe, machinery, heavy equipment, freight, or fixtures requires special handling, Tenant agrees to employ only persons holding a master rigger's license to do said work, and that all work in connection therewith shall comply with applicable laws and regulations. Any such moving shall be at the sole risk and hazard of Tenant and Tenant hereby agrees to exonerate, indemnify and save Landlord harmless against and from any liability, loss, injury, claim or suit resulting directly or indirectly from such moving. Tenant shall schedule such moving at such times as Landlord shall reasonably designate.

6.2.4 Electricity. Tenant shall not connect to the electrical distribution system serving the Premises a total load exceeding the lesser of the capacity of such system or the maximum load permitted from time to time under applicable governmental regulations. The capacity of the electrical distribution system serving the Premises shall be the lesser of (a) the

capacity of the branch of the system serving the Premises exclusively or (b) Tenant's Percentage of the capacity of the system serving the entire Building.

6.2.5 Installation, Alterations or Additions. Tenant shall not make any installations, alterations, additions or improvements (collectively and individually referred to in this paragraph as "work" or "Alterations") in, to or on the Premises nor permit the making of any holes in the walls, partitions, ceilings or floors without on each occasion obtaining the prior consent of Landlord, and then only pursuant to plans and specifications approved by Landlord in advance in each instance. Landlord's approval shall not be unreasonably withheld, conditioned or delayed with respect to work that does not materially affect the structural elements of the Building, equals or exceeds Building standards in quality, and is not reasonably anticipated to adversely affect the mechanical, electrical, plumbing, HVAC or life-safety systems of the Building in such a manner so as to impact other tenants or occupants of the Building, is not visible from outside of the Premises and shall not increase Taxes or Operating Costs.
Notwithstanding the foregoing, Tenant need not obtain Landlord's consent to perform Cosmetic Alterations within the Premises so long as Tenant shall give Landlord at least five (5) Business Days' prior notice thereof (which shall reasonably describe the work), and any such work shall be scheduled at a time reasonably acceptable to Landlord and Tenant. "Cosmetic alterations" shall mean work that (a) is of a cosmetic nature such as painting, wallpapering, hanging pictures and installing carpeting; (b) is not visible from the exterior of the Premises or Building; (c) does not require work to be performed inside the walls or above the ceiling of the Premises or below the floor of the Premises; (d) does not materially affect the Building's structure or base Building systems; and (e) do not require a building permit. In addition Tenant may, without Landlord's consent and without prior notice to Landlord (except to schedule access to freight elevators, loading docks or any other common areas or facilities) install readily removable business equipment, business fixtures and work stations in the Premises. All work to be performed to the Premises by Tenant shall (i) be performed in a good and workmanlike manner by contractors approved in advance by Landlord, which approval shall not be unreasonably withheld,
conditioned or delayed, provided that Landlord may require Tenant to engage Landlord's designated contractors for work affecting the roof and/or fire and life safety systems of the Building, and in compliance with the provisions of Exhibit C and all applicable zoning, building, fire, health and other codes, regulations, ordinances and laws and in compliance with the U.S.
Environmental Protection Agency's Energy Star tenant space criteria and the Tenant Design and Construction Guidelines set forth in Exhibit G, as same may be amended from time to time, (ii) be made at Tenant's sole cost and expense and at such times and in such a manner as Landlord may from time to time reasonably designate, and (iii) be free of liens and encumbrances and become part of the Premises and the property of Landlord without being deemed additional rent for tax purposes, Landlord and Tenant agreeing that Tenant shall be treated as the owner of the work for tax purposes until the expiration or earlier termination of the term hereof, subject to Landlord's rights pursuant to Subsection 6.1.9 to require Tenant to remove the same at or prior to the expiration or earlier termination of the term hereof and, to the extent Landlord shall make such election, title thereto shall remain vested in Tenant at all times. Tenant shall pay promptly when due the entire cost of any work to the Premises so that the Premises, Building and Property shall at all times be free of liens, and, at Landlord's request, Tenant shall furnish to Landlord a bond or other security acceptable to Landlord assuring that any such work will be completed in accordance with the plans and specifications theretofore approved by Landlord and assuring that the Premises will remain free of any mechanics' lien or other encumbrances that may arise out of

such work. Prior to the commencement of any such work, Tenant shall cause its general contractor to execute and deliver an agreement in the form attached hereto as Exhibit D, and Tenant shall, throughout any such work, maintain, or cause to be maintained, the insurance required by Exhibit D, or such other coverages or limits as shall be reasonably required by Landlord. In addition, Tenant shall save Landlord harmless and indemnified from all injury, loss, claims or damage to any person or property occasioned by or arising out of such work. Whenever and as often as any mechanic's or materialmen's lien shall have been filed against the Property based upon any act of Tenant or of anyone claiming through Tenant, Tenant shall within five (5) Business Days of notice from Landlord to Tenant take such action by bonding, deposit or payment as will remove or satisfy the lien. Tenant shall at the end of the term, upon written request of Landlord, execute and deliver to Landlord a bill of sale covering any work Tenant shall be required to surrender hereunder.

Tenant shall not, at any time, directly or indirectly, employ or permit the employment of any contractor, mechanic or laborer in the Premises, if such employment will interfere or cause any conflict with other contractors, mechanics or laborers engaged in the construction, maintenance or operation of the Building by Landlord, Tenant or others. In the event of any such interference or conflict, Tenant, upon demand of Landlord, shall cause all contractors, mechanics or laborers causing such interference or conflict to leave the Building immediately.

Tenant's restoration obligations with respect to any alterations is as provided in Subsection 6.1.9.

6.2.6 Abandonment. Tenant shall not abandon the Premises during the term; provided that, so long as Tenant otherwise fulfills its obligations under this Lease including, without limitation, its obligations to pay Annual Fixed Rent and all Additional Rent and its maintenance and repair obligations, Tenant shall have the right to vacate the Premises.

6.2.7 Signs. Tenant shall not paint or place any signs or place any curtains, blinds, shades, awnings, aerials, or the like, visible from outside the Premises. Landlord shall not unreasonably withhold consent for signs or lettering on or adjacent to the entry doors to the Premises provided such signs conform to building standards adopted by Landlord and Tenant has submitted to Landlord a plan or sketch of the sign to be placed on such entry doors. Landlord agrees, however, to maintain a tenant directory in the lobby of the Building in which will be placed Tenant's name and the location of the Premises in the Building.

So long as (i) this Lease is still in full force and effect and (ii) Ultragenyx Pharmaceutical Inc. (or, its subtenants, assignees, including but not limited to any successor by Merger, or any Affiliate (the "Sign Conditions"), occupy at least fifty percent (50%) of the rentable area of the Building, Tenant shall have the non-exclusive right, subject to applicable legal requirements and the terms of this Lease, at Tenant's sole cost and expense, to install and maintain a single building-mounted sign (hereinafter, "Tenant's Sign") on the uppermost façade of the Building, which Tenant's Sign, subject to receipt of applicable permits and approvals, shall face Chestnut Street. The size, construction, location and design of Tenant's Sign shall be subject to Landlord's approval, not to be unreasonably withheld, conditioned or delayed. Without limiting the foregoing, Landlord may refuse to approve any sign that is not consistent with the architecture and general appearance of the Building and Property, will cause undue damage to

the Building, or which is otherwise inconsistent with first-class office building signage. The content of Tenant's Sign shall be limited to Tenant's name or trade name or business logo. Tenant, at its expense, shall obtain all permits and approvals required for the installation of Tenant's Sign prior to the installation thereof (but shall not be permitted to seek any zoning or similar relief for Tenant's Sign without Landlord's consent, which may be withheld in Landlord's sole discretion), and shall keep all such permits and approvals in full force and effect throughout the term. Tenant acknowledges that Tenant's Sign shall be at Tenant's risk and Tenant shall maintain Tenant's Sign in good condition. The installation, repair, maintenance and removal of Tenant's Sign shall be subject to the provisions of Subsection 6.2.5 of this Lease and Landlord's other reasonable requirements. Landlord reserves the right, upon reasonable notice to Tenant, to require Tenant to remove Tenant's Sign, temporarily, at Landlord's sole cost and expense, if necessary in connection with any repairs, renovations, improvements or additions to the Building, provided that Landlord shall minimize, to the extent practical, the duration of any period during which Tenant's Sign shall need to be removed. Prior to the expiration or earlier termination of the term of this Lease, and if at any time any of the Sign Conditions shall no longer prevail, Tenant shall remove Tenant's Sign (and all associated hardware) from the Building and shall restore the affected area to the condition existing prior to the installation of Tenant's Sign.

6.2.8 Oil and Hazardous Materials. Except as provided herein, Tenant shall not introduce on or transfer to the Premises or Property, any Hazardous Materials (as hereinafter defined); nor dump, flush or otherwise dispose of any Hazardous Materials into the drainage, sewage or waste disposal systems serving the Premises or Property; nor generate, store, use, release, spill or dispose of any Hazardous Materials in or on the Premises or the Property, or transfer any Hazardous Materials from the Premises to any other location; and Tenant shall not commit or suffer to be committed in or on the Premises or Property any act which would require any reporting or filing of any notice with any governmental agency pursuant to any statutes, laws, codes, ordinances, rules or regulations, present or future, applicable to the Property or to Hazardous Materials.

Tenant agrees that if it shall generate, store, release, spill, dispose of or transfer to the Premises or Property any Hazardous Materials, it shall forthwith remove the same, at its sole cost and expense, in the manner provided by all applicable Environmental Laws (as hereinafter defined), regardless of when such Hazardous Materials shall be discovered. Furthermore, Tenant shall pay any fines, penalties or other assessments imposed by any governmental agency with respect to any such Hazardous Materials and shall forthwith repair and restore any portion of the Premises or Property which it shall disturb in so removing any such Hazardous Materials to the condition which existed prior to Tenant's disturbance thereof.

Tenant agrees to deliver promptly to Landlord any notices, orders or similar documents received from any governmental agency or official concerning any violation of any Environmental Laws or with respect to any Hazardous Materials affecting the Premises or Property. In addition, Tenant shall, within ten (10) days of receipt, accurately complete any questionnaires from Landlord or other informational requests relating to Tenant's use of the Premises and, in particular, to Tenant's use, generation, storage and/or disposal of Hazardous Materials at, to, or from the Premises.

Tenant shall indemnify, defend (by counsel satisfactory to Landlord), protect, and hold Landlord free and harmless from and against any and all claims, or threatened claims, including without limitation, claims for death of or injury to any person or damage to any property, actions, administrative proceedings, whether formal or informal, judgments, damages, punitive damages, liabilities, penalties, fines, costs, taxes, assessments, forfeitures, losses, expenses, attorneys' fees and expenses, consultant fees, and expert fees that arise from or are caused in whole or in part, directly or indirectly, by (i) Tenant's use, analysis, storage, transportation, disposal, release, threatened release, discharge or generation of Hazardous Materials to, in, on, under, about or from the Premises, or (ii) Tenant's failure to comply with any Environmental Laws. Tenant's obligations hereunder shall include, without limitation, and whether foreseeable or unforeseeable, all costs (including, without limitation, capital, operating and maintenance costs) incurred in connection with any investigation or monitoring of site conditions, repair, cleanup, containment, remedial, removal or restoration work, or detoxification or decontamination of the Premises, and the preparation and implementation of any closure, remedial action or other required plans in connection therewith. For purposes of this Section 6.2.8, any acts or omissions of Tenant, or its subtenants or assignees or its or their employees, agents, or contractors (whether or not they are negligent, intentional, willful or unlawful) shall be attributable to Tenant.

The term "Hazardous Materials" shall mean and include any oils, petroleum products, asbestos, radioactive, biological, medical or infectious wastes or materials, and any other toxic or hazardous wastes, materials and substances which are defined, determined or identified as such in any Environmental Laws, or in any judicial or administrative interpretation of Environmental Laws.

The term "Environmental Laws" shall mean any and all federal, state and municipal statutes, laws, regulations, ordinances, rules, judgments, orders, decrees, codes, plans, injunctions, permits, concessions, grants, franchises, licenses, agreements or other governmental restrictions relating to the environment or to emissions, discharges or releases of pollutants, contaminants, petroleum or petroleum products, medical, biological, infectious, toxic or hazardous substances or wastes into the environment including, without limitation, ambient air, surface water, ground water or land, or otherwise relating to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or handling of pollutants, contaminants, petroleum or petroleum products, medical, biological, infectious, toxic or hazardous substances or wastes or the cleanup or other remediation thereof.

6.2.9 Hazardous Materials Documents. Landlord acknowledges that it is not the intent of this Subsection 6.2.9 to prohibit Tenant from operating its business for the Permitted Uses. Tenant may operate its business according to the custom of Tenant's industry so long as the use or presence of Hazardous Materials is strictly and properly monitored in accordance with applicable laws. As a material inducement to Landlord to allow Tenant to use Hazardous Materials in connection with its business, (i) prior to the Commencement Date Tenant shall deliver to Landlord a list identifying each type of Hazardous Material to be present at the Premises that is subject to regulation under any environmental applicable laws and (ii) within ten (10) days following Landlord's request, to be made if required by Landlord's lender or prospective lender, any prospective purchaser of the Building or any governmental authority, or if Landlord has a reasonable basis to believe Tenant is not operating in compliance with such approvals or permits or otherwise not in compliance with Environmental Laws, a list of any and

all approvals or permits from governmental authorities required in connection with the presence of such Hazardous Material at the Premises (collectively, "Hazardous Materials Documents"). Tenant shall deliver to Landlord updated Hazardous Materials Documents (a) within thirty (30) days after receipt of a request therefor from Landlord, but not more often than once per year, and
(b) if there are any material increases to the amounts or changes to the types of Hazardous Materials used in connection with Tenant's business in the Premises. For each type of Hazardous Material listed, the Hazardous Materials Documents shall include (t) the chemical name, (u) the material state (e.g., solid, liquid, gas or cryogen), (v) the concentration, (w) the storage amount and storage condition (e.g., in cabinets or not in cabinets), (x) the use amount and use condition (e.g., open use or closed use), (y) the location (e.g., room number or other identification) and (z) if known, the chemical abstract service number. Notwithstanding anything in this Subsection 6.2.9 to the contrary, Tenant shall not be required to provide Landlord with any Hazardous Materials Documents to the extent containing information of a proprietary nature. Landlord shall keep the Hazardous Materials Documents confidential; provided, however, Landlord may, at Landlord's expense, cause the Hazardous Materials Documents to be reviewed by a person or firm qualified to analyze Hazardous Materials to confirm compliance with the provisions of this Lease and with applicable laws, so long as Landlord notifies such person or firm of the confidential nature of the Hazardous Materials Document and such person or firm agrees, in writing and subject to applicable law, to keep such information confidential. In the event that a review of the Hazardous Materials Documents indicates non-compliance with this Lease or applicable laws, Tenant shall, at its expense, diligently take steps to bring its storage and use of Hazardous Materials into compliance. Tenant shall deliver to Landlord, prior to installation thereof, correct and complete copies of plans relating to the installation of any storage tanks to be installed in, on, under or about the Property by Tenant (provided that installation of storage tanks shall only be permitted after Landlord has given Tenant its written consent to do so, which consent Landlord may withhold in its sole and absolute discretion) and closure plans or any other documents required by any and all governmental authorities for any storage tanks installed in, on, under or about the Property by a Tenant for the closure of any such storage tanks.

6.2.10 Exit Survey. At least five (5) Business Days (and not more than sixty (60) days) prior to the expiration or earlier termination of the term of this Lease, Tenant shall provide Landlord with a facility decommissioning and Hazardous Materials closure plan for the Premises ("Exit Survey") prepared by an independent third party reasonably acceptable to Landlord. The Exit Survey shall comply with the American National Standards Institute's Laboratory Decommissioning guidelines (ANSI/AIHA Z9.11-2008) or any successor standards published by ANSI or any successor organization (or, if ANSI and its successors no longer exist, a similar entity publishing similar standards). In addition, at least ten (10) days (and not more than sixty (60) days) prior to the expiration or earlier termination of the term of this Lease, Tenant shall provide Landlord with written evidence of all appropriate governmental releases obtained by Tenant in accordance with applicable laws, including laws pertaining to the surrender of the Premises. Tenant's obligations under this Section shall survive the expiration or earlier termination of the Lease.

6.2.11 Odors and Exhaust. Tenant agrees as follows:

(i) Tenant shall not cause or permit (or conduct any activities that would cause) any release of any noxious or reasonably objectionable odors or fumes of any kind from the Premises due to Tenant's operations.

(ii) Tenant shall, at Tenant's sole cost and expense, provide odor eliminators and other devices (such as filters, air cleaners, scrubbers and whatever other equipment may in Landlord's reasonable judgment be necessary or appropriate from time to time) to remove, eliminate and abate any odors, fumes or other substances in Tenant's exhaust stream that, in Landlord's reasonable judgment, emanate from the Premises. Any work Tenant performs under this Section shall constitute Alterations (as that term is defined in Exhibit C attached hereto).

(iii) Tenant's responsibility to remove, eliminate and abate noxious or reasonably objectionable odors, fumes and exhaust shall continue throughout the term. Landlord's approval of any Alterations or other tenant improvements or construction of any work to be performed by Landlord in the Premises shall not preclude Landlord from reasonably requiring additional measures to eliminate odors, fumes and other adverse impacts of Tenant's exhaust stream (as Landlord may designate in Landlord's reasonable discretion). Tenant shall install additional equipment as Landlord reasonably requires from time to time under the preceding sentence. Such installations shall constitute Alterations.

(iv) If Tenant fails to install satisfactory odor control equipment within thirty (30) days (or such longer period as may be reasonably required provided Tenant is diligently pursuing such installation) after Landlord's demand made at any time, then Landlord may, without limiting Landlord's other rights and remedies, require Tenant to cease and suspend any operations in the Premises that, in Landlord's reasonable determination, cause odors or fumes. For example, if Landlord reasonably determines that Tenant's production of a certain type of product causes odors or fumes, and Tenant does not install satisfactory odor control equipment within thirty (30) days after Landlord's request or such longer period as may be reasonably required provided Tenant is diligently pursuing such installation, then Landlord may require Tenant to stop producing such type of product in the Premises unless and until Tenant has installed odor control equipment reasonably satisfactory to Landlord.

Notwithstanding anything to the contrary contained in this Lease, during the Term, Tenant shall be entitled to Tenant's pro rata share of the maximum allowable chemical quantities (both in use and in storage) permitted by MAQ Codes (defined below) for the second (2nd) floor of the Building, which maximum allowable chemical quantities for the entire second (2nd) floor is 360 liquid gallons, subject to Tenant maintaining all licenses, permits and approvals required therefor, which pro rata share, as of the Date of this Lease, is 67% of the maximum allowable chemical quantities. As used herein, "MAQ Codes" shall mean 780 CMR – Massachusetts State Building Code 9th Edition, 527 CMR – Massachusetts Comprehensive Fire Safety Code, and NEPA 45 – Standard on Fire Protection for Laboratories Using Chemicals, 2011 Edition.

## Article 7
## Casualty or Taking

7.1 Termination. In the event that the Premises or the Property, or any material part thereof, shall be taken by any public authority or for any public use (other than temporarily for a

period of less than one hundred eighty (180) days) or shall be condemned by the action of any public authority, then the term of this Lease may be terminated at the election of Landlord by giving written notice thereof to Tenant within one hundred (120) days after the date of the taking or condemnation. In the event that the Premises or the Property, or any material part thereof shall be destroyed or damaged by fire or casualty, then within a reasonable period of time of casualty, not to exceed ninety (90) days after the occurrence of such casualty damage, Landlord shall deliver to Tenant the written estimate (as reasonably estimated by an architect or general contractor selected by Landlord) of the time to substantially complete the restoration of the Premises and the Property to the substantially the same as existed immediately prior to such damage (subject to any modification required by then current laws, rules, regulations and ordinances and excluding any improvements to the Premises made by or on behalf of Tenant after the Commencement Date) (the "Restoration Estimate"). If the Restoration Estimate provides that such restoration period is greater than one hundred eighty (180) days, then the term of this Lease may be terminated at the election of Landlord. Such election, which may be made notwithstanding the fact that Landlord's entire interest may have been divested, shall be made by the giving of notice by Landlord to Tenant ("Landlord's Restoration Notice") not later than one hundred twenty (120) days after the date of the taking or casualty.

In the event that all or any material portion of the Premises is, in Tenant's sole judgement, made unusable for the conduct of Tenant's business due to a taking or condemnation by any public authority (other than temporarily for a period of less than one hundred eighty (180) days), then the term of this Lease may be terminated at the election of Tenant by giving written notice thereof to Landlord within one hundred twenty (120) days after the date of the taking or condemnation. In the event that all or any material part of the Premises shall be destroyed or damaged or shall be made inaccessible or unusable for the conduct of Tenant's business, in Tenant's sole judgement, by fire or other casualty (and Landlord has not elected to terminate the term of this Lease pursuant to the preceding paragraph), and, if (a) the Restoration Estimate indicates that the time required to substantially complete such restoration work shall exceed one hundred and eighty (180) days from the occurrence of such casualty damage or the number of days which as of the date of the casualty constitutes more than half of the then remainder of the term, whichever period is shorter, or (b) Landlord's Restoration Notice indicates that Landlord shall not restore the Premises as provided above, then Tenant may elect to terminate the term of this Lease by giving written notice to Landlord not later forty-five (45) days after the date on which Landlord delivers Landlord's Restoration Notice to Tenant. Tenant may also elect to terminate the term of this Lease by written notice to Landlord if Landlord shall not have caused the restoration work to have been substantially completed on or before the date thirty (30) days after the date identified in the Restoration Estimate, subject to extension for Force Majeure, whereupon the term of this Lease shall terminate thirty (30) days following the date of such notice, unless Landlord substantially completes such restoration work with such thirty (30) day period, in which case such notice of termination shall be a nullity. Notwithstanding the foregoing, Tenant shall have no right to terminate the term of this Lease due to a fire or other casualty if the cause thereof was due to the gross negligence or intentional misconduct of Tenant or any subtenant of Tenant or any agent or employee of Tenant or its subtenant(s).

7.2 Restoration. If neither party so elects to terminate, this Lease shall continue in force and (so long as the damage is not caused by the gross negligence or other wrongful act of Tenant or its employees, agents, contractors or invitees) a just proportion of the Annual Fixed

Rent reserved, according to the nature and extent of the damages sustained by the Premises, shall be suspended or abated until the Premises (excluding any improvements to the Premises made at Tenant's expense), or what may remain thereof, shall be put by Landlord in proper condition for use, which Landlord covenants to do with reasonable diligence to the extent permitted by the net proceeds of insurance recovered or damages awarded for such destruction, taking, or condemnation and subject to zoning and building laws or ordinances then in existence. Landlord shall keep Tenant reasonably informed as to the status of such restoration work. "Net proceeds of insurance recovered or damages awarded" refers to the gross amount of such insurance or damages actually made available to Landlord (and not retained by any Superior Lessor or Superior Mortgagee) less the reasonable expenses of Landlord incurred in connection with the collection of the same, including without limitation, fees and expenses for legal and appraisal services.

7.3 Award. Irrespective of the form in which recovery may be had by law, all rights to seek reimbursement for damages or compensation arising from fire or other casualty or any taking by eminent domain or condemnation shall belong to Landlord in all cases. Tenant hereby grants to Landlord all of Tenant's rights to such claims for damages and compensation and covenants to deliver such further assignments thereof as Landlord may from time to time request. Nothing contained herein shall be construed to prevent Tenant from prosecuting in any condemnation proceedings a claim for relocation expenses, provided that such action shall not affect the amount of compensation otherwise recoverable by Landlord from the taking authority.

## Article 8
## Defaults

8.1 Default of Tenant. (a) (I) If Tenant shall default in its obligations to pay the Annual Fixed Rent or regularly scheduled payments of Additional Rent under this Lease when due, or if Tenant shall default in its obligations to pay any invoice for Additional Rent or any other charges or amounts under this Lease when due and if any such default shall continue for seven (7) days after notice from Landlord designating such default, or (II) shall default in complying with its obligations under Sections 4.4 or 6.1.11 of this Lease and if any such default shall continue for five (5) days after notice from Landlord designating such default, or (III) if as promptly as possible but in any event within thirty (30) days after notice from Landlord to Tenant specifying any default or defaults other than those set forth in clauses (I) or (II) Tenant has not cured the default or defaults so specified, or if such default is of such a nature that it cannot be cured within thirty (30) days using diligent efforts, if Tenant does not commence the curing of such default within such thirty-day period and thereafter diligently and continuously prosecute such cure to completion within such additional time as may be necessary, but in no event to exceed ninety (90) days from the date of Landlord's notice to Tenant specifying the default (which 90-day period shall be extended on a day for day basis for each day that Tenant's cure is delayed solely due to Force Majeure events or Landlord-cause delays); or (b) if any assignment shall be made by Tenant for the benefit of creditors; or (c) if Tenant's leasehold interest shall be taken on execution; or (d) if a lien or other involuntary encumbrance shall be filed against Tenant's leasehold interest or Tenant's other property, including said leasehold interest, and shall not be discharged within ten (10) days thereafter; or (e) if a petition shall be filed by Tenant for liquidation, or for reorganization or an arrangement under any provision of

any bankruptcy law or code as then in force and effect; or (f) if an involuntary petition under any of the provisions of any bankruptcy law or code shall be filed against Tenant and such involuntary petition shall not be dismissed within thirty (30) days thereafter; or (g) if a custodian or similar agent shall be authorized or appointed to take charge of all or substantially all of the assets of Tenant; or (h) if Tenant dissolves or shall be dissolved or shall liquidate or shall adopt any plan or commence any proceeding, the result of which is intended to include dissolution or liquidation; or (i) if any order shall be entered in any proceeding by or against Tenant decreeing or permitting the dissolution of Tenant or the winding up of its affairs; or (j) if Tenant shall fail to pay any installment of rent when due, Tenant shall cure such default within the grace period provided in clause (a) (I) above (or with Landlord's approval after the expiration of such grace period) and Tenant shall, within the next year following the date such initial defaulted payment was first due, fail more than once to pay any installment of Annual Fixed Rent or Additional Rent when due, then, and in any of such cases indicated in clauses (a) through (j) hereof (collectively and individually, a "Default of Tenant"), Landlord may, in addition to and not in derogation of any remedies for any preceding breach of covenant, immediately or at any time thereafter (x) give notice to Tenant terminating this Lease and/or the term hereof, which notice shall specify the date of such termination, whereupon on the date so specified, the term of this Lease and all of Tenant's rights and privileges under this Lease shall expire and terminate or (y) without terminating this Lease terminate Tenant's right of possession and/or occupancy and reenter and take possession of the Premises or any part thereof, without notice and expel Tenant and any party claiming under Tenant and remove any of their effects, without being liable on account thereof, whether in trespass or breach or covenant or otherwise, (and no such reentry or taking possession shall be construed as an election by Landlord to terminate this Lease unless Landlord shall affirm such election by notice expressly to such effect), but in either case Tenant shall remain liable as hereinafter provided.

8.2 Remedies. In the event of any termination of this Lease or the term hereof pursuant to Section 8.1, Tenant shall pay the Annual Fixed Rent, Additional Rent and other charges payable hereunder up to the time of such termination. Thereafter, whether or not the Premises shall have been re-let, Tenant shall be liable to Landlord for, and shall pay to Landlord the Annual Fixed Rent, Additional Rent and other charges which would be payable hereunder for the remainder of the term of this Lease had such termination not occurred, less the net proceeds, if any, of any reletting of the Premises, after deducting all expenses in connection with such reletting, including, without limitation, all repossession costs, brokerage commissions, attorneys' fees and expenses, advertising costs, administration expenses, alteration costs, the value of any tenant inducements (including but without limitation free rent, moving costs, and contributions toward leasehold improvements) and any other expenses incurred in preparation for such reletting. Tenant shall pay such damages to Landlord monthly on the days on which the Annual Fixed Rent, Additional Rent or other charges would have been payable hereunder if the term of this Lease had not been so terminated.

In the event of any reentry or retaking of possession of the Premises and/or termination of Tenant's right of possession and/or occupancy of the Premises, as applicable, without termination of this Lease, pursuant to Section 8.1, Tenant shall pay the Annual Fixed Rent, Additional Rent and other charges payable hereunder up to the time of such reentry or retaking of possession and/or termination. Thereafter, whether or not the Premises shall have been re-let, Tenant shall be liable to Landlord for, and shall pay to Landlord the Annual Fixed Rent, Additional Rent and

other charges which would be payable hereunder for the remainder of the term of this Lease notwithstanding any such reentry, retaking of possession or termination, less the net proceeds, if any, of any reletting of the Premises, after deducting all expenses in connection with such
reletting, including, without limitation, all repossession costs, brokerage commissions, attorneys' fees and expenses, advertising costs, administration expenses, alteration costs, the value of any tenant inducements (including but without limitation free rent, moving costs, and contributions toward leasehold improvements) and any other expenses incurred in preparation for such reletting. Tenant shall pay such damages to Landlord monthly on the days on which the Annual Fixed Rent, Additional Rent or other charges are payable hereunder.

At any time after any such termination, reentry or retaking of possession, in lieu of recovering damages pursuant to the provisions of the immediately preceding paragraphs with respect to any period after the date of demand therefor, at Landlord's election, Tenant shall pay to Landlord immediately the amount, if any, by which (A) the Annual Fixed Rent, Additional Rent and other charges which would be payable hereunder from the date of such demand to the end of what would be the then unexpired term of this Lease had such termination not occurred (or in the case of reentry or retaking of possession of the Premises by Landlord or a termination of Tenant's right of possession and/or occupancy of the Premises, to the end of the term of this Lease), shall exceed (B) the then fair rental value of the Premises for the same period, reduced to amortize over such period all costs or expenses which Landlord would incur to obtain such fair market rent. In calculating any excess amount under the prior sentence, the amounts under (A) and (B) of the prior sentence shall be first discounted to their net present value using a discount rate equal to eight percent (8%).

Nothing contained in this Lease shall, however, limit or prejudice the right of 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, the damages are to be proved, whether or not the amount be greater than, equal to, or less than the amount of the loss or damages referred to above.

In case of any Default of Tenant, re-entry, expiration and repossession by summary proceedings or otherwise, Landlord may (i) relet the Premises or any part or parts thereof, either in the name of Landlord, Tenant (Tenant hereby irrevocably appointing Landlord its attorney in fact to execute any instrument of reletting on behalf of Tenant) or otherwise (as Landlord may elect), for a term or terms which may at Landlord's option be equal to or less than or exceed the
period the balance of the term of this Lease (or the balance of the term of this Lease if it shall not have been terminated) and may grant concessions or free rent to the extent that Landlord considers advisable and necessary to relet the same and (ii) may make such commercially reasonable alterations and repairs in the Premises as Landlord in its reasonable discretion considers advisable and necessary for the purpose of reletting the Premises; and the making of such alterations and repairs shall not operate or be construed to release Tenant from liability hereunder as aforesaid. Subject to Landlord's obligations in Subsection 8.2.21 below, Landlord shall in no event be liable in any way whatsoever for failure to relet the Premises, or, in the event that the Premises are relet, for failure to collect the rent under such reletting.

To the fullest extent permitted by law, Tenant hereby expressly waives any and all rights of redemption granted under any present or future laws in the event of Tenant being evicted or dispossessed, or in the event of Landlord obtaining possession of the Premises, by reason of the violation by Tenant of any of the covenants and conditions of this Lease.

8.2.1 Landlord's Mitigation. Following a termination of the term of this Lease due to a Default of Tenant and the surrender of the Premises to Landlord in the condition required by this Lease, Landlord shall, to the extent (if any) required by applicable law, use reasonable efforts to mitigate its damages hereunder.

8.3 Remedies Cumulative. Except as expressly provided otherwise in Section 8.2, any and all rights and remedies which Landlord may have under this Lease, and at law and equity (including without limitation actions at law for direct, indirect, special and consequential (foreseeable and unforeseeable) damages), for Tenant's failure to comply with its obligations under this Lease shall be cumulative and shall not be deemed inconsistent with each other, and any two or more of all such rights and remedies may be exercised at the same time insofar as permitted by law.

Notwithstanding the foregoing, to the fullest extent permitted by law, Landlord hereby waives, and Tenant shall not be liable to Landlord for, any claim for special or consequential losses or damages (excluding, for purposes of clarity, damages to which Landlord may be entitled under Section 8.2) arising out of any breach of this Lease by Tenant, except for any damages to which Landlord may be entitled under Section 8.5 and provided that the foregoing waiver shall not apply to any violation by Tenant of Environmental Laws or any claims asserted by a third party for which Landlord may be liable as a result, in whole or part, of conduct constituting a breach by Tenant of any of the terms of this Lease.

8.4 Landlord's Right to Cure Defaults. At any time with or without notice, Landlord shall have the right, but shall not be required, to pay such sums or do any act which requires the expenditure of monies which may be necessary or appropriate by reason of the failure or neglect of Tenant to comply with any of its obligations under this Lease (irrespective of whether the same shall have ripened into a Default of Tenant), and in the event of the exercise of such right by Landlord, Tenant agrees to pay to Landlord forthwith upon demand, as Additional Rent, all such sums including reasonable attorney's fees, together with interest thereon at a rate (the "Default Rate") equal to the lesser of six hundred basis points above the Prime Rate or the maximum rate allowed by law. "Prime Rate" shall mean the annual floating rate of interest, determined daily and expressed as a percentage from time to time announced by Bank of America as its "prime" or "base" rate, so-called, or if at any time Bank of America ceases to announce such a rate, as announced by the largest national or state-chartered banking institution then having an office in the City of Boston and announcing such a rate. If at any time neither Bank of America nor the largest national or state-chartered banking institution having an office in the City of Boston is announcing such a floating rate, "Prime Rate" shall mean a rate of interest, determined daily, which is two hundred basis points above the yield of 90-day U.S. Treasury Bills.

8.5 Holding Over. Any failure by Tenant to comply timely with its obligations under Subsection 6.1.9, as to all or any portion of the Premises, shall constitute a holding over of the

entire Premises and be treated as a daily tenancy at sufferance at a rental rate equal 125% of the sum of Annual Fixed Rent plus Additional Rent on account of Operating Costs and Taxes in effect immediately prior to the expiration or earlier termination of the term (prorated on a daily basis) for the first thirty (30) days of any such holding over and 150% of the sum of Annual Fixed Rent plus Additional Rent on account of Operating Costs and Taxes in effect immediately prior to the expiration or earlier termination of the term (prorated on a daily basis) thereafter.
Tenant shall also pay to Landlord all damages, direct and/or consequential (foreseeable and unforeseeable), sustained by reason of any such holding over, provided that Tenant shall not be liable for consequential damages unless Tenant shall hold over for more than thirty (30) days. Otherwise, all of the covenants, agreements and obligations of Tenant applicable during the term of this Lease shall apply and be performed by Tenant during such period of holding over as if such period were part of the term of this Lease.

8.6 Effect of Waivers of Default. Any consent or permission by Landlord to any act or omission by Tenant shall not be deemed to be consent or permission by Landlord to any other similar or dissimilar act or omission and any such consent or permission in one instance shall not be deemed to be consent or permission in any other instance.

8.7 No Waiver, etc. The failure of Landlord or Tenant to seek redress for violation of, or to insist upon the strict performance of, any covenant or condition of this Lease shall not be deemed a waiver of such violation nor prevent a subsequent act, which would have originally constituted a violation, from having all the force and effect of an original violation. The receipt by Landlord of rent with knowledge of the breach of any covenant of this Lease shall not be deemed to have been a waiver of such breach by Landlord, or by Tenant, unless such waiver be in writing signed by the party to be charged. No consent or waiver, express or implied, by Landlord or Tenant to or of any breach of any agreement or duty shall be construed as a waiver or consent to or of any other breach of the same or any other agreement or duty.

8.8 No Accord and Satisfaction. No acceptance by Landlord of a lesser sum than the Annual Fixed Rent, Additional Rent or any other charge then due shall be deemed to be other than on account of the earliest installment of such rent or charge due, nor shall any endorsement or statement on any check or any letter accompanying any check or payment as rent or other charge be deemed an accord and satisfaction, and Landlord may accept such check or payment without prejudice to Landlord's right to recover the balance of such installment or pursue any other remedy in this Lease provided.

## Article 9
## Rights of Holders

9.1 Rights of Mortgagees or Ground Lessor. On the condition Landlord shall perform its obligations under Section 9.3, this Lease, and all rights of Tenant hereunder, are and shall be subject and subordinate to any ground or master lease, and all renewals, extensions, modifications and replacements thereof, and to all mortgages, which may now or hereafter affect the Building or the Property and/or any such lease, whether or not such mortgages shall also cover other lands and/or buildings and/or leases, to each and every advance made or hereafter to be made under such mortgages, and to all renewals, modifications, replacements and extensions

of such leases and such mortgages and all consolidations of such mortgages. This Section shall be self-operative and no further instrument of subordination shall be required. In confirmation of such subordination, Tenant shall promptly execute, acknowledge and deliver any instrument in form and substance reasonably satisfactory to Tenant that Landlord, the lessor under any such lease or the holder of any such mortgage or any of their respective successors in interest may reasonably request to evidence such subordination provided Landlord shall have performed its obligations under Section 9.3. Any lease to which this Lease is subject and subordinate is herein called "Superior Lease" and the lessor of a Superior Lease or its successor in interest, at the time referred to, is herein called "Superior Lessor"; and any mortgage to which this Lease is subject and subordinate, is herein called "Superior Mortgage" and the holder of a Superior Mortgage is herein called "Superior Mortgagee".

9.2 Modifications. If any Superior Lessor or Superior Mortgagee shall require any modification(s) of this Lease, Tenant shall, at Landlord's request, promptly execute and deliver to Landlord such instruments effecting such modification(s) as Landlord shall require, provided that such modification(s) do not adversely affect any of Tenant's monetary rights or monetary obligations under this Lease or have more than a de minimis impact on Tenant's non-monetary rights or non-monetary obligations under this Lease. In addition, and notwithstanding Section
9.1 to the contrary, any Superior Lessor or Superior Mortgagee may, at its option, subordinate the Superior Lease or Superior Mortgage of which it is the lessor or holder to this Lease by giving Tenant ten (10) days prior written notice of such election, whereupon this Lease shall, irrespective of dates of execution, delivery and recording, be superior to such Superior Lease or Superior Mortgage and no other documentation shall be necessary to effect such change.

9.3 Non-Disturbance. As of the Date of this Lease, Landlord represents and warrants that there are no Superior Leases affecting the Premises, Building or Property. As of the Date of this Lease, Landlord represents and warrants that there are no Superior Mortgages affecting the Premises, Building or Property other than that certain mortgage by Landlord in favor of SM Tactical Finance III-B LLC (the "Existing Lender"), as successor-in-interest to SM Tactical Finance III LLC. Concurrently with the execution of this Lease, Landlord shall obtain and deliver to Tenant a so-called subordination, non-disturbance and attornment agreement ("SNDA") from the Existing Lender (provided the Existing Lender shall still be the holder of a Superior Mortgage and Tenant shall, at Landlord's election, first execute and deliver such agreement to Landlord) which shall be in the form attached hereto as Exhibit J. Tenant's subordination of its leasehold interest under this Lease to any Superior Lessor or Superior Mortgagee shall be subject to and conditioned upon such future Superior Lessor or Superior Mortgagee entering into an SNDA with Tenant, which may be in the form customarily used by such Superior Lessor or Superior Mortgagee, or if no such form exists, in any commercially reasonable form, subject to the conditions and limitations of Sections 9.1 and 9.2, provided that, at Landlord's election, Tenant shall first execute and deliver such agreement to Landlord.

## Article 10
## Miscellaneous Provisions

10.1 Notices. Except as may be expressly provided herein otherwise, all notices, requests, demands, consents, approval or other communications to or upon the respective parties

hereto shall be in writing, shall be delivered by hand or mailed by certified or registered mail, return receipt requested, or by a nationally recognized courier service that provides a receipt for delivery such as Federal Express, United Parcel Service or U.S. Postal Service Express Mail and shall be addressed as follows: If intended for Landlord, to the Original Address of Landlord set forth in Section 1.1 of this Lease with a copy to Sullivan & Worcester LLP, One Post Office Square, Boston, MA 02119 Attn: Sharon G. Leifer, Esq. (or to such other address or addresses as may from time to time hereafter be designated by Landlord by notice to Tenant); and if intended for Tenant, addressed to Tenant at the Original Address of Tenant set forth in Section 1.1 of this Lease, with a copy to Tenant c/o Ultragenyx Pharmaceutical Inc., 60 Leveroni Court, Novato, CA 94949, Attention: Finance Department (or to such other address or addresses as may from time to time hereafter be designated by Tenant by notice to Landlord). Notices shall be effective on the date delivered to (or the first date such delivery is attempted and refused by) the party to which such notice is required or permitted to be given or made under this Lease. Notices from
Landlord may be given by Landlord's Agent, if any, or Landlord's attorney; and any bills or invoices for Annual Fixed Rent or Additional Rent may be given by mail (which need not be registered or certified) and, if so given, shall be deemed given on the third Business Day following the date of posting.

10.2 Quiet Enjoyment; Landlord's Right to Make Alterations, Etc. Landlord agrees that upon Tenant's paying the rent and performing and observing the agreements, conditions and other provisions on its part to be performed and observed, Tenant shall and may peaceably and quietly have, hold and enjoy the Premises during the term hereof without any manner of hindrance or molestation from Landlord or anyone claiming under Landlord, subject, however, to the terms of this Lease; provided, however, Landlord reserves the right at any time and from
time to time, without the same constituting breach of Landlord's covenant of quiet enjoyment or an actual or constructive eviction, and without Landlord incurring any liability to Tenant or otherwise affecting Tenant's obligations under this Lease, to make such changes, alterations, improvements, repairs or replacements in or to the interior and exterior of the Building (including the Premises) and the fixtures and equipment thereof, and in or to the Property, or properties adjacent thereto, as Landlord may deem necessary or desirable, and to change (provided that there be no unreasonable obstruction of the right of access to the Premises by Tenant and that Landlord use commercially reasonable efforts to minimize, to the extent practical, any interference with the conduct of business at the Premises) the arrangement and/or location of entrances or passageways, doors and doorways, corridors, elevators, or other common areas of the Building and Property.

Without incurring any liability to Tenant, Landlord may permit access to the Premises and open the same, whether or not Tenant shall be present, upon any demand of any receiver, trustee, assignee for the benefit of creditors, sheriff, marshal or court officer Landlord reasonably believes is entitled to such access for the purpose of taking possession of, or removing, Tenant's property or for any other lawful purpose (but this provision and any action by Landlord hereunder shall not be deemed a recognition by Landlord that the person or official making such demand has any right or interest in or to this Lease, or in or to the Premises), or upon demand of any representative of the fire, police, building, sanitation or other department of the city, state or federal governments.

10.3 Lease not to be Recorded; Confidentiality of Lease Terms. Tenant agrees that it will not record this Lease. Both parties shall, upon the request of either (and at the expense of the requesting party), execute and deliver a notice or short form of this Lease in such form, if any, as may be acceptable for recording with the Middlesex County (Southern District) Registry of Deeds. In no event shall such document set forth the rent or other charges payable by Tenant pursuant to this Lease; and any such document shall expressly state that it is executed pursuant to the provisions contained in this Lease and is not intended to vary the terms and conditions of this Lease.

Tenant acknowledges that the terms under which the Landlord has leased the Premises to Tenant (including, without limitation, the rental rate(s), term and other financial and business terms), constitute confidential information of Landlord ("Confidential Information"). Tenant covenants and agrees to keep the Confidential Information confidential and not to disclose the same to third parties; provided, however, that such Confidential Information may be disclosed by Tenant to those of its officers, employees, attorneys, accountants, lenders and financial advisors (collectively, "Representatives") who need to know such information in connection with
Tenant's use and occupancy of the Premises and for financial reporting and credit related activities. Tenant shall not make or permit to be made any press release or other similar public statement regarding this Lease without the prior approval of Landlord, which approval shall not be unreasonably withheld. Tenant furthermore agrees to inform its Representatives of the confidential nature of such Confidential Information and to use all reasonable efforts to cause each Representative to treat such Confidential Information confidentially and in accordance with the terms of this paragraph.

10.4 Assignment of Rents and Transfer of Title; Limitation of Landlord's Liability. Tenant agrees that the assignment by Landlord of Landlord's interest in this Lease, or the rents payable hereunder, whether absolute or conditional in nature or otherwise, which assignment is
made to the holder of a mortgage on property which includes the Premises, shall never be treated as an assumption by such holder of any of the obligations of Landlord hereunder unless such holder shall, by notice sent to Tenant, specifically otherwise elect and that, except as aforesaid, such holder shall be treated as having assumed Landlord's obligations hereunder (subject to the
limitations set forth in Section 9.1) only upon foreclosure of such holder's mortgage and the taking of possession of the Premises.

The term "Landlord", so far as covenants or obligations to be performed by Landlord are concerned, shall be limited to mean and include only the owner or owners at the time in question of Landlord's interest in the Property, and in the event of any transfer or transfers of such title to said property, Landlord (and in case of any subsequent transfers or conveyances, the then grantor) shall be concurrently freed and relieved from and after the date of such transfer or conveyance, without any further instrument or agreement, of all liability with respect to the performance of any covenants or obligations on the part of Landlord contained in this Lease thereafter to be performed, it being intended hereby that the covenants and obligations contained in this Lease on the part of Landlord, shall, subject as aforesaid, be binding on Landlord, its successors and assigns, only during and in respect of their respective period of ownership of such interest in the Property.

Notwithstanding the foregoing, in no event shall the acquisition of Landlord's interest in the Property by a purchaser which, simultaneously therewith, leases Landlord's entire interest in the Property back to Landlord or the seller thereof be treated as an assumption by operation of law or otherwise, of Landlord's obligations hereunder. Tenant shall look solely to such seller-lessee, and its successors from time to time in title, for performance of Landlord's obligations hereunder. The seller-lessee, and its successors in title, shall be the Landlord hereunder unless and until such purchaser expressly assumes in writing the Landlord's obligations hereunder.

Tenant shall not assert nor seek to enforce any claim for breach of this Lease against any of Landlord's assets other than Landlord's interest in the Property, including Landlord's interest in the rents payable by tenants of the Building, Landlord's interest in the proceeds of any insurance maintained by Landlord or Tenant with respect to the Property or the Premises, and Landlord's interest in the proceeds from the sale of the Property, and Tenant agrees to look solely to such interest for the satisfaction of any liability or claim against Landlord under this Lease, it being specifically agreed that in no event whatsoever shall Landlord ever be personally liable for any such liability. Tenant furthermore agrees that no trustee, officer, director, general or limited partner, member, shareholder, beneficiary, employee or agent of Landlord (including any person or entity from time to time engaged to supervise and/or manage the operation of Landlord) shall be held to any liability, jointly or severally, for any debt, claim, demand, judgment, decree, liability or obligation of any kind (in tort, contract or otherwise) of, against or with respect to Landlord or arising out of any action taken or omitted for or on behalf of Landlord.

10.5 Landlord's Default. Landlord shall not be deemed to be in breach of, or in default in the performance of, any of its obligations under this Lease unless it shall fail to perform such obligation(s) and such failure shall continue for a period of thirty (30) days, or such additional time as is reasonably required to correct any such breach or default, after written notice has been given by Tenant to Landlord specifying the nature of Landlord's alleged breach or default; provided, however, that the notice and cure period set forth in this sentence shall not apply to any failure to deliver the Premises to Tenant by February 28, 2024 (i.e., one hundred eighty (180) days after the Delivery Date) for reasons other than Force Majeure or Tenant Delay. Except as provided in Section 3.1, Tenant shall have no right to terminate this Lease for any breach or default by Landlord hereunder and no right, for any such breach or default, to offset or counterclaim against any rent due hereunder. Except as provided in Section 3.1 with regards to damages incurred by Tenant under the Existing Lease, in no event shall Landlord ever be liable to Tenant, and Tenant hereby waives any claim against Landlord, for any punitive damages or for any loss of business or any other indirect, special or consequential damages suffered by Tenant from whatever cause. Tenant further agrees that if Landlord shall have failed to cure any such breach or default within thirty (30) days of such notice to Landlord (or if such breach or default cannot be cured within said time, then within such additional time as may be necessary if within said thirty days Landlord has commenced and is diligently pursuing the remedies necessary to cure such breach or default), then the holder(s) of any mortgage(s) or the lessor under any ground lease entitled to notice pursuant to Section 10.6 shall have an additional thirty (30) days within which to cure such breach or default if such breach or default cannot be cured within that time, then such additional time as may be necessary, if within such thirty (30) days any such holder or lessor has commenced and is diligently pursuing the remedies necessary to

cure such breach or default (including but not limited to commencement of foreclosure proceedings, if necessary to effect such cure).

10.6 Notice to Mortgagee and Ground Lessor. After receiving notice from any party that it holds a mortgage which includes the Premises as part of the mortgaged premises, or that it is the ground lessor under a lease with Landlord, as ground lessee, which includes the Premises as part of the demised premises, no notice from Tenant to Landlord shall be effective unless and until a copy of the same is given to such holder or ground lessor, and the curing of any of
Landlord's defaults by such holder or ground lessor shall be treated as performance by Landlord.

10.7 Brokerage. Tenant and Landlord warrant and represent that they have dealt with no broker in connection with the consummation of this Lease, other than CBRE, Inc. and Newmark, and in the event of any brokerage claims or liens, other than by CBRE, Inc. and/or Newmark, against Landlord, Tenant or the Property predicated upon or arising out of prior dealings with Tenant or Landlord, the party with whom the broker claims to have dealt agrees to defend the same and indemnify and hold the other party harmless against any such claim, and to discharge any such lien.

10.8 Waiver of Jury Trial. LANDLORD AND TENANT HEREBY WAIVE TRIAL BY JURY IN ANY ACTION, PROCEEDING OR COUNTERCLAIM BROUGHT BY EITHER OF THEM AGAINST THE OTHER IN CONNECTION WITH THIS LEASE.

10.9 Applicable Law and Construction. This Lease shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts and if any provisions of this Lease shall to any extent be invalid, the remainder of this Lease shall not be affected thereby. This Lease may be executed in multiple counterparts, including by electronic signature or DocuSign, each of which shall constitute an original instrument but all of which shall constitute one and the same agreement. Tenant expressly acknowledges and agrees that Landlord has not made and is not making, and Tenant, in executing and delivering this Lease, is not relying upon, any warranties, representations, promises or statements, except to the extent that the same are expressly set forth in this Lease or in any other written agreement which may be made between the parties concurrently with the execution and delivery of this Lease and which shall expressly refer to this Lease. All understandings and agreements heretofore made between the parties are merged in this Lease and any other such written agreement(s) made concurrently herewith, which alone fully and completely express the agreement of the parties and which are entered into after full investigation, neither party relying upon any statement or representation not embodied in this Lease or any other such written agreement(s) made concurrently herewith. This Lease may be amended, and the provisions hereof may be waived or modified, only by instruments in writing executed by Landlord and Tenant. The titles of the several Articles and Sections contained herein are for convenience only and shall not be considered in construing this Lease. The submission of this document for examination and negotiation does not constitute an offer to lease, or a reservation of, or option for, the Premises, and Tenant shall have no right to the Premises hereunder until the execution and delivery hereof by both Landlord and Tenant. Except as herein otherwise provided, the terms hereof shall be binding upon and shall inure to the benefit of the successors and assigns, respectively, of Landlord and Tenant and, if Tenant shall be an individual, upon and to his heirs, executors, administrators, successors and assigns. Each term and each provision of this Lease to be

performed by Tenant shall be construed to be both an independent covenant and a condition and time is of the essence with respect to the exercise of any of Tenant's rights, and the performance of any and all of Tenant's obligations, under this Lease. The reference contained to successors and assigns of Tenant is not intended to constitute a consent to assignment by Tenant. Except as otherwise set forth in this Lease, any obligations of Tenant (including, without limitation, rental and other monetary obligations, repair and maintenance obligations and obligations to indemnify Landlord), shall survive the expiration or earlier termination of this Lease, and Tenant shall immediately reimburse Landlord for any expense incurred by Landlord in curing Tenant's failure to satisfy any such obligation (notwithstanding the fact that such cure might be effected by Landlord following the expiration or earlier termination of this Lease).

10.10 Tenant's Authority. Tenant represents that any individual executing this Lease on behalf of Tenant is authorized to do so.

10.11 Roof Equipment. Tenant, at its sole cost and expense and subject to all applicable laws, codes and regulations and the provisions of this Section 10.11, may install on the roof of the Building and/or in the penthouse area of the Building and operate during the term antennae and other communications equipment, supplemental HVAC equipment and other roof-top equipment serving the Premises ("Roof Equipment") of the type customarily installed on the roofs of laboratory and office buildings comparable to the Building by tenants occupying premises therein devoted exclusively to laboratory and office uses similar to the Permitted Uses; provided that (a) the aggregate amount of space on the roof that shall be allocated to Tenant for Tenant's Roof Equipment shall be four hundred (400) square feet and (b) the aggregate amount of space in the penthouse (on a per square foot basis) that shall be allocated to Tenant for Tenant's Roof Equipment shall be equal to Tenant's Percentage of the maximum rentable area of the penthouse, which is ninety-six (96) rentable square feet; and provided further that the location of Tenant's Roof Equipment (i.e., on the roof or in the penthouse) shall be reasonably determined by Landlord in cooperation with Tenant. Tenant also shall have the right to run cables and lines ("Lines") from its Roof Equipment to the Premises using the common shafts, chases, risers and conduits of the Building intended for such purpose to the extent that the same may be available after meeting Landlord's requirements for the Building. Landlord makes no representations, express or implied, that the roof of the Building is suitable for the installation or operation of any Roof Equipment. There shall be no additional charge to Tenant in connection with its use of space on the roof of the Building, but Tenant shall pay Annual Fixed Rent for so much of the penthouse space as Tenant elects to use at a rate per rentable square foot of such penthouse space per annum equal to the lesser of (i) the market rental rate at which Landlord is then offering penthouse space to third parties or (ii) the Annual Fixed Rent per rentable square foot of penthouse space per annum being paid by other tenants of the Building. If Tenant elects to install any equipment in the penthouse area, Tenant shall notify Landlord of the amount of space required not later than the third (3rd) anniversary of the Commencement Date, time being of the essence, and promptly following receipt of such notice the parties shall execute an amendment to this Lease providing for the addition of such penthouse space to the Premises (it being agreed that after the third (3rd) anniversary of the Commencement Date, Tenant shall be entitled to lease only such space as may then be available in the penthouse, and such space may or may not be equal to Tenant's Percentage of the maximum rentable area of the penthouse).

All Roof Equipment shall be subject to Landlord's approval, which, subject to Landlord's customary practices and procedures, shall not be unreasonably withheld, conditioned or delayed. The design and installation of Tenant's Roof Equipment shall be performed in accordance with Subsection 6.2.5 and Exhibit C, any requirements of Landlord's insurance carrier(s), and all other applicable provisions of this Lease as if the area where the Roof Equipment is located were part of the Premises. Tenant agrees that Landlord may require Tenant to reasonably screen its Roof Equipment.

Landlord shall have no obligation to furnish any utilities or services to the Roof Equipment or to make any alterations, repairs or replacements to any portion of the Building or Property in order to accommodate the installation or operation of any Roof Equipment. All utilities required to operate the Roof Equipment shall be separately metered and Tenant shall pay the costs of such utilities, as measured by such meter(s) to Landlord, as Additional Rent, or directly to the utility supplier. Tenant agrees that it shall be required, at is sole cost and expense, to perform any roof reinforcement reasonably required by Landlord to accommodate the weight of any Roof Equipment on the Building roof. Under no circumstances shall Tenant make any roof penetrations other than as expressly approved by Landlord in writing in advance.

During the term, Tenant shall, at its sole cost and expense, perform all repairs and maintenance to the Roof Equipment and Lines necessary to keep the same in good working order, appearance and condition, reasonable use and wear thereof excepted, and Tenant shall promptly repair any damage to the Building or Property caused by the installation or operation of the Roof Equipment or Lines. Tenant shall operate its Roof Equipment in compliance with all applicable laws, codes and regulations. Tenant shall not relocate or modify any of the Roof Equipment or Lines without, in each instance, obtaining Landlord's prior written approval to such relocation or modification.

Any antennae installed by Tenant on the Building roof shall provide communications for Tenant only, and Tenant shall not permit any other person or firm to make use thereof.

Unless Landlord shall agree otherwise in writing, Tenant shall, prior to the expiration or earlier termination of the term of this Lease, remove all of its Roof Equipment and all Lines, repair any damage caused by such removal, and restore the portion of the roof where the Roof Equipment was installed to a condition substantially the same as existed prior to the installation of the Roof Equipment. The provisions of Subsection 6.1.9 shall apply to any area affected hereby as if it were part of the Premises.

Landlord reserves the right, upon not less than thirty (30) days' notice to Tenant, except in the event of an emergency, but at Landlord's cost, to require Tenant to relocate all or any of the Roof Equipment to another portion of the roof reasonably designated by if such relocation is necessary for Landlord to perform any repairs, renovations, improvements or additions to the Building or Property. Landlord shall use reasonable efforts to coordinate any such relocation with Tenant.

Tenant shall be entitled to obtain access to the roof both during and outside of Normal Building Operating Hours (as defined in the Rules and Regulations) for the purpose of servicing Tenant's Roof Equipment, but only if (i) Tenant shall have given Landlord reasonable advance

notice of the need therefor, and (ii) Tenant is accompanied by an authorized representative of Landlord during such access. Any such access shall be subject to Landlord's reasonable security measures and, in the event access is required before or after Normal Building Operating Hours, Landlord may require Tenant to pay, as Additional Rent, the reasonable costs incurred by Landlord to provide such access to Tenant.

Tenant shall use reasonable efforts to not allow any antennae or other Roof Equipment installed by Tenant to interfere with any equipment installed or operating in or from the Building as of the date Tenant commences operation of, or shall subsequently modify, such Roof Equipment. If Landlord determines that any of Tenant's Roof Equipment materially interferes any such pre-existing equipment, Landlord may require Tenant to discontinue operation of such Roof Equipment until such time as it may be operated without causing such interference.

10.12 Prevailing Parties. If either Landlord or Tenant should bring suit (or alternate dispute resolution proceedings) against the other with respect to this Lease including, without limitation, for unlawful detainer, forcible entry and detainer, or any other relief against the other hereunder, then all reasonable and actual costs and expenses incurred by the prevailing party in a final, nonappealable action therein (including its actual appraisers', accountants', attorneys' and other professional fees, expenses and court costs), shall be paid by the other party, including any and all costs incurred in enforcing, perfecting and executing such judgment and all reasonable costs and attorneys' fees associated with any appeal.

[Remainder of page intentionally left blank.]

WITNESS the execution hereof under seal on the day and year first above written.

Landlord:

BRICKBOTTOM I QOZB LP

By: NRL Manager LLC
Its general
partner

By: North River Company, LLC Its
Manager

By: /s/ Christopher S. Flagg
Name: Christopher S. Flagg
Title: Manager

Tenant:

Ultragenyx Pharmaceutical Inc.

By: /s/ Emil Kakkis
Name: Emil Kakkis Title: CEO

**Exhibit 21.1**

**Significant Subsidiaries of Ultragenyx Pharmaceutical Inc.**

| Name of Subsidiary | Jurisdiction of Incorporation |
|---|---|
| Ultragenyx Holdco LLC | Delaware |
| Rare Delaware Inc. | Delaware |
| GeneTx Biotherapeutics 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 |
| Ultragenyx Japan K.K. | Japan |

**Exhibit 23.1**

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-8 Nos. 333-194773, 333-201843, 333-209729, 333-216110, 333-223124, 333-229746, 333-236428, 333-253007, and 333-262751) pertaining to the 2011 Equity Incentive Plan, as amended, 2014 Incentive Plan, as amended, 2014 Employee Stock Purchase Plan, as amended, and Employee Inducement Plan of Ultragenyx Pharmaceutical Inc.,

(2) 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., and

(3) Registration Statement (Form S-3 No. 333-253008) and related Prospectus of Ultragenyx Pharmaceutical Inc. for the registration of common stock, preferred stock, debt securities, warrants and units;

of our reports dated February 16, 2023, 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, 2022.

/s/ Ernst & Young LLP

San Mateo, California
February 16, 2023

**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. I am 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. 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 16, 2023

/s/ Emil D. Kakkis

Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer and 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, 2022 (the "Report"), I, Emil D. Kakkis, M.D., Ph.D., as President and Chief Executive Officer 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 16, 2023

/s/ Emil D. Kakkis

Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer and Principal Financial Officer)