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 , 2024
OR
TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

☐

For the transition period from to
Commission File No. 001-36276

Ultragenyx Pharmaceutical Inc.

(Exact name of registrant as specified in its charter)

Delaware	**27-2546083**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
60 Leveroni Court	
Novato , California	**94949**
(Address of principal executive offices)	*(Zip Code)*

(415) 483-8800
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the 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 ☐ N O ☑

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. Y ES ☑ 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.

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

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. ☑
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). ☐

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Company as of June 30, 2024 was approximately $

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, 2025, the Company had

92,501,126

shares of common stock issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2025 Annual Meeting of Stockholders, to be held on or about May 15, 2025, 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 "aim", “anticipate,” “believe,” “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, or commercialization of, 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, including our expectations for profitability for 2027, and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- developments and projections relating to our competitors and our industry;
- stagnating or worsening business and economic conditions and increasing geopolitical instability, including inflationary pressures, general economic slowdown or a recession, high interest rates, foreign exchange rate volatility, financial institution instability, and changes in monetary policy;
- the impact of market conditions and volatility on unrealized gains or losses on our nonqualified deferred compensation plan investments and our financial results; 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 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 such 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 committed to bringing novel products to patients for the treatment of serious rare and ultrarare genetic diseases. We have built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are typically no approved therapies treating the underlying disease.

We were founded in April 2010 by our President and Chief Executive Officer, Emil Kakkis, M.D., Ph.D., and are led by a management team experienced in the development and commercialization of rare disease therapeutics. Our strategy is predicated upon time- and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency.

Our Strategy

The critical components of our business strategy include the following:

- ***Focus on rare and ultrarare genetic diseases with significant unmet medical need and clear biology.*** There are numerous rare and ultrarare 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, adeno-associated virus, or AAV, 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, AAV 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 pipeline of clinical product candidates:

Products	Description	Indication	Phase 1	Phase 2	Phase 3	Approved
Biologics						
Crysvita® (burosumab)[1]	Fully human monoclonal antibody	XLH				
Crysvita® (burosumab)[1]	Fully human monoclonal antibody	TIO				
Mepsevii® (vestronidase alfa)	Enzyme replacement	MPSVII				
Evkeeza® (evinacumab)[2]	Fully human monoclonal antibody	HoFH				
UX143 (setrusumab)[3]	Fully human monoclonal antibody	OI				
Small Molecules						
Dojolvi® (triheptanoin)	Substrate replacement	LC-FAOD				
AAV Gene Therapy						
UX111 (rebisufligene etisparvovec)	AAV9 Gene Therapy	MPS IIIA				
DTX401 (pariglasgene brecaparvovec)	AAV8 Gene Therapy	GSDIa				
DTX301 (avalotcagene ontaparvovec)	AAV8 Gene Therapy	OTC				
UX701 (rivunatpagene miziparvovec)	AAV9 Gene Therapy	Wilson				
Nucleic Acid						
GTX-102	Antisense Oligonucleotide	Angelman Syndrome				

1: In collaboration with Kyowa Kirin Company
2: In collaboration outside of the US with Regeneron Pharmaceuticals
3: In collaboration with Mereo BioPharma

Approved Products

Crysvita for the treatment of X-Linked Hypophosphatemia, or XLH, and Tumor-Induced Osteomalacia, or TIO

Crysvita is a fully human monoclonal antibody administered via subcutaneous injection, that targets fibroblast growth factor 23, or FGF23, developed for the treatment of XLH. XLH is 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 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, 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 Kirin Co., Ltd." for a description of our collaboration and license agreement with KKC.

Mepsevii for the treatment of Mucopolysaccharidosis VII, or MPS VII

Mepsevii is an enzyme replacement therapy administered intravenously, or IV, that replaces the missing enzyme (beta-glucuronidase), developed for the treatment of MPS VII or Sly syndrome. MPS VII is 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 Long-chain Fatty Acid Oxidation Disorders, or LC-FAOD

Dojolvi is a highly purified, synthetic, 7-carbon fatty acid triglyceride administered orally, designed to provide medium-chain, odd-carbon fatty acids as an energy source and metabolite replacement, developed for people with LC-FAOD. LC-FAOD represents 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.

In November 2024, we announced that we had received a positive finalized assessment report with agreement to file for Conditional Early Approval, or CEA, from Japan's Pharmaceuticals and Medical Devices Agency, or PMDA, based on the currently available global clinical data for the product. With this feedback, we expect to file a Japan-New Drug Application for CEA in mid-2025.

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 Homozygous Familial Hypercholesterolemia, or HoFH

Evkeeza is a fully human monoclonal antibody administered by IV, that binds to and blocks the function of angiopoietin-like 3, or ANGPTL3, a protein that plays a key role in lipid metabolism, developed for the treatment of HoFH, a rare inherited condition. HoFH occurs when two copies of the genes causing familial hypercholesterolemia are inherited, one from each parent, resulting in dangerously high levels (>400 mg/dL) of low-density lipoprotein-cholesterol, or LDL-C, which is 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, Brazil and Japan as a first-in-class therapy for use together with diet and other LDL-C lowering therapies. In these regions, Evkeeza is generally approved to treat adults and adolescents aged five 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.

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

Clinical Product Candidates

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

UX143 (setrusumab) is a fully human monoclonal antibody administered by IV 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 developed for the treatment of OI, or brittle bone disease, which is caused by variants in the *COL1A1* or *COL1A2* genes, leading to either reduced or abnormal collagen and changes in bone metabolism. There are an estimated 60,000 patients in the developed world affected by OI. UX143 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 and Breakthrough Designation from the FDA, and was accepted into the EMA's Priority Medicines, or PRIME, program. Setrusumab is subject to our collaboration agreement with Mereo and is the lead clinical asset in our bone endocrinology franchise.

In April 2024, we announced all patients in the Phase 3 *Orbit* and *Cosmic* studies had been enrolled. The Phase 3 portion of *Orbit* enrolled 159 patients and is a randomized placebo-controlled study evaluating the effect of setrusumab compared to placebo on the rate of annualized clinical fractures in patients aged five to less than 25 years. *Cosmic* enrolled 69 patients and is an active-controlled study evaluating the effect of setrusumab compared to intravenous bisphosphonate, or IV-BP, therapy on annualized total fracture rate in patients aged two to less than seven years.

In June 2024, we announced positive 14-month results from the Phase 2 portion of the ongoing Phase 2/3 *Orbit* study demonstrating that, as of a May 24, 2024 data cut-off date, treatment with setrusumab continued to show statistically significant reductions in the incidence of fractures in patients with OI compared to the pre-treatment period. Treatment with setrusumab also resulted in ongoing and meaningful improvements in lumbar spine bone mineral density, or BMD, at month 12 without evidence of plateau.

As we announced in June 2024, the median annualized rate of radiologically confirmed fractures across all 24 patients in the two years prior to treatment was 0.72. Following a mean treatment duration period of 16 months, the median annualized fracture rate was reduced 67% to 0.00 ($p=0.0014$; $n=24$). The reduction in annualized fracture rates was associated with continued, clinically meaningful increases in BMD. Tests conducted at the 12-month timepoint demonstrated that treatment with setrusumab resulted in a mean increase in lumbar spine BMD from baseline of 22% ($p<0.0001$, $n=19$) across all age groups (five to less than 26 years old), a further improvement from 14% observed at six months of treatment. This increase in BMD is reflected in the change from the mean baseline lumbar spine BMD Z-score of -1.73 to -0.49 at 12 months across all age groups, a substantial normalization in Z-score of +1.25 ($p<0.0001$, $n=18$). This is further improved from the mean six-month Z-score change of +0.85. The improvements in BMD and Z-scores were statistically significant and consistent across all OI sub-types studied.

As of the May 24, 2024 data cut-off, there were no treatment-related serious adverse events observed in the study. Reported adverse events were generally consistent with those observed in the *Asteroid* study with infusion-related events and headache determined to be the most common adverse events related to the study drug. As of the data cut-off, there were no reported hypersensitivity reactions related to setrusumab.

In January 2025, we announced that the Phase 3 *Orbit* study is progressing to the second interim analysis expected in mid-2025. Patients in the *Cosmic* study also continue to be treated with either setrusumab or IV-BP therapy and will be evaluated in parallel with the second *Orbit* interim analysis in mid-2025 and final analyses, if needed, in the fourth quarter of 2025.

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, administered by intrathecal injection that inhibits expression of the paternal *UBE3A* antisense. GTX-102 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 and has been accepted into the EMA's PRIME program.

In January 2024, we announced that enrollment in the Expansion Cohorts had been completed in the Phase 1/2 study of GTX-102 for the treatment of Angelman syndrome. Across the Phase 1/2, including the Dose Escalation and Expansion Cohorts, there are a total of 74 patients enrolled in the Phase 1/2 study.

In April 2024, we presented interim data from the Phase 1/2 study at the 76th Annual American Academy of Neurology Meeting. Patients in Expansion Cohorts A & B treated with GTX-102 showed rapid and clinically meaningful improvement across multiple domains consistent with or exceeding Dose Escalation Cohorts 4-7 data at Day 170. Treatment of the Dose Escalation Cohorts 4-7 showed long-term increasing and sustained clinical benefit far exceeding Natural History data at Day 758.

In December 2024, we announced that enrollment began in the global Phase 3 *Aspire* study, which is expected to enroll approximately 120 children ages four to 17 with Angelman syndrome with a genetically confirmed diagnosis of full maternal UBE3A gene deletion. Participants will be randomized 1:1 to receive GTX-102 by intrathecal injection via lumbar puncture or to the sham comparator group during the 48-week primary efficacy analysis period. The primary endpoint will be improvement in cognition assessed by Bayley-4 cognitive raw score, and the key secondary endpoint (with a 10% allocation of alpha) will be the Multi-domain Responder Index across the five domains of cognition, receptive communication, behavior, gross motor function, and sleep. Enrollment in the Phase 3 *Aspire* study is expected to complete in the second half of 2025.

The Phase 2/3 *Aurora* study, which will evaluate GTX-102 in other Angelman syndrome genotypes and ages, is expected to initiate in 2025.

Please see "—License and Collaboration Agreements—Clinical Product Candidates—GeneTx" for a description of our license agreement with GeneTx Biotherapeutics LLC, or GeneTx.

UX111 (rebisufligene etisparvovec) 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, administered by a one-time IV infusion that provides the cross-correcting enzyme that enables the breakdown of Heparan sulfate, or HS. UX111 is being developed 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 program was acquired through an exclusive license agreement with Abeona Therapeutics, or Abeona, that was announced in May 2022. 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 December 2024, we submitted a BLA to the FDA for UX111 supported by the available data, including from the ongoing pivotal Transpher A study. New clinical data were presented at WORLDSymposium™ 2025 in February 2025, that demonstrated treatment with UX111 led to a statistically significant improvement in the Bayley-III raw scores for the subdomains of cognition, receptive communication and expressive communication in patients with MPS IIIA compared to Natural History Data from untreated patients. These clinical endpoints were correlated with substantial and sustained reduction in levels of heparan sulfate in cerebrospinal fluid.

The FDA granted the BLA Priority Review with a Prescription Drug User Fee Act, or PDUFA, action date of August 18, 2025.

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

DTX401 (pariglasgene brecaparvovec) for the treatment of Glycogen Storage Disease Type Ia, or GSDIa

DTX401 is an adeno-associated virus 8, or AAV8, gene therapy clinical candidate, administered by a one-time IV infusion that is designed to deliver stable expression and activity of G6Pase-α, an essential enzyme in glycogen and glucose metabolism. DTX401 is being developed for the treatment of patients with GSDIa, and is the most common genetically inherited glycogen storage disease, with an estimated 6,000 patients in the developed world. A Pediatric Investigation Plan, or PIP, was accepted by the EMA. The DTX401 program has received Rare Pediatric Disease, RMAT, Fast Track, and Orphan Drug designations in the U.S., and PRIME and Orphan Medicinal Product Designations in the EU.

In May 2024, we announced positive topline results from our Phase 3 *GlucoGene* study for the treatment of patients aged eight years and older. The study achieved its primary endpoint, demonstrating that treatment with DTX401 resulted in a statistically significant and clinically meaningful reduction in daily cornstarch intake compared with placebo at Week 48.

In November 2024, we provided updated, longer-term Phase 3 data. After the 48-week primary efficacy analysis period, crossover patients (previously treated with placebo) were eligible to receive DTX401. As of the data cut-off, 12 crossover patients had reached Week 30 post-treatment and had a substantial 61.6% mean reduction of daily cornstarch at this early timepoint, double the rate of decrease when compared to patients in the original DTX401 treatment arm (n=20) at week 30 and that showed a mean 41.3% reduction at the end of the 48-weeks. Patients from the original DTX401 treatment arm who had reached 78 weeks are continuing to reduce their daily cornstarch intake, while maintaining glycemic control. DTX401 has demonstrated a consistent and acceptable safety profile with no new safety concerns identified as of the data cut-off.

These results have been discussed with regulatory authorities in a pre-BLA meeting and will be included as part of a BLA submission in mid-2025.

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

DTX301 (avalotcagene ontaparvovec) for the treatment of Ornithine Transcarbamylase, or OTC, deficiency

DTX301 is an AAV8 gene therapy product candidate, administered by a one-time IV infusion that is designed to deliver stable expression and activity of the *OTC*, gene. DTX301 is being developed for the treatment of patients with OTC deficiency, which 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 February 2025, we announced enrollment had been completed in the Phase 3 study of DTX301 for the treatment of OTC deficiency with a total of 37 patients randomized 1:1 to DTX301 or placebo. The co-primary endpoints are the percentage of patients who achieve a response as measured by the change in 24-hour plasma ammonia levels and discontinuation or reduction ammonia-scavenger medications and protein-restricted diet. Based on an amended protocol, the change in 24-hour ammonia levels will be measured through Week 36, after which the study would unblind and patients will be followed for a total of up to 64 weeks to determine the complete responders able to move safely to both ammonia-scavenger medications and protein-restricted diet control.

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

UX701 (rivunatpagene miziparvovec) for the treatment of Wilson Disease

UX701 is an AAV type 9 gene therapy, administered by a one-time IV infusion that is designed to deliver a truncated form of the *ATP7B* gene. UX701 is being developed for the treatment of patients with Wilson disease, which affects more than 50,000 patients 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.

In February 2024, we announced that we enrolled and dosed 15 patients in the three dose escalating cohorts of the first, dose-finding, stage of the pivotal *Cyprus2*+ study of UX701 for the treatment of Wilson disease. During Stage 1, the safety and efficacy of UX701 is being evaluated across three, sequential dosing cohorts (Cohort 1: 5.0 x 10^12 GC/kg Cohort 2: 1.0 x 10^13 GC/kg and Cohort 3: 2.0 x 10^13 GC/kg).

In October 2024, we shared that UX701 demonstrated clinical activity in the pivotal *Cyprus2*+study as well as improvements in copper metabolism for patients treated in Stage 1. Multiple responders had completely tapered off standard-of-care treatment with responses seen in all three dose cohorts. In Stage 1, 15 patients were enrolled into the three sequential dosing cohorts and followed for at least 24 weeks. Six of the patients completely tapered off of standard-of-care treatment with chelators and/or zinc therapy, and a seventh patient had begun tapering as of the data cut-off date in August 2024. In patients who had tapered off standard-of-care, non-ceruloplasmin bound copper (NCC) had stabilized to normal, healthy levels. In some patients, there were increases in ceruloplasmin-copper activity consistent with improved *ATP7b* function. UX701 has been well tolerated, with no unexpected related treatment-emergent adverse events and no significant immunologic safety events as of the data cut-off.

We expect to enroll a fourth cohort in Stage 1 at a moderately increased dose and with an optimized immunomodulation regimen to enhance the efficiency and efficacy of the gene therapy, with the objective of having the majority of patients come off standard-of-care treatment before selecting a dose for the randomized placebo-controlled stage of the study. Enrollment in Cohort 4 is expected to begin in the first half of 2025 and expected to complete in the second half of 2025.

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

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 by a competitor 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. Although we are not aware of any other products currently in clinical development for the treatment of 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. Competitors could also enter the market with generic versions of Dojolvi. As described in “Item 3. Legal Proceedings” below, in 2024, Navinta LLC (Navinta), Aurobindo Pharma Limited, Aurobindo Pharma USA, Inc., or collectively, Aurobindo, Esjay Pharma Private Limited and Esjay Pharma LLC, or collectively, Esjay, filed ANDAs seeking FDA approval to market a generic version of Dojolvi.

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, we are aware of other clinical development programs that target ANGPTL 3 across various indications including HoFH, including from Arrowhead Pharmaceuticals, zodasiran an siRNA, Eli Lilly/Dicerna, solbinsiran an siRNA, Novo Nordisk, NNC0491-6075 an antibody, and CRISPR Therapeutics, CTX-301 a gene editor.

With respect to UX143, there are currently no approved drugs for OI. Most pediatric patients with OI 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 3 clinical testing by Amgen.

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 preclinical and clinical development programs for Angelman syndrome, including Phase 2 programs from Ionis, ION582 an ASO, and Neuren Pharmaceuticals, NNZ-2591 an IGF-1 analog.

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 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. We are also aware of enzyme replacement therapies, including DNL126, in Phase 1/2 by Denali, and JR-441, in Phase 1/2 by JCR Pharma.

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, we are aware of other clinical development programs for OTC deficiency including from Arcturus Therapeutics, ARCT-810 a mRNA, Bloomsbury, BGT-OTCD a gene therapy, and iECURE, ECUR-506 a gene editor.

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 a chelator, ALXN-1840, that is in Phase 3 for Wilson disease by Monopar Therapeutics.

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 were the lead party for development activities in the Profit-Share Territory and in the European Territory until the applicable transition date. We shared 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 was the transition date for the Profit-Share Territory, KKC became the lead party and became 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 shared 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 Crysvita in Latin America and Turkey.

In the Profit-Share Territory, KKC booked sales of products and we had 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 was five years from commercial launch. The parties subsequently agreed that we would have the right to continue to support KKC in commercial field activities in the U.S. through January 31, 2025, as amended. After January 31, 2025, our rights to promote Crysvita in the U.S. are limited to medical geneticists and we solely bear our expenses for the promotion of Crysvita in the Profit-Share Territory. See “Item I.A. Risk Factors” for additional information on the risks related to our dependency on KKC for the commercialization of 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. In Latin America, we book sales of products and have the sole right to promote and sell the products.

Under the collaboration agreement, KKC manufactures and supplies Crysvita for sales in Latin American territories and we pay KKC a transfer price of 30% of net sales. We also pay KKC a low single-digit royalty on net sales in Latin America. The remaining profit or loss from commercializing products in the Profit-Share Territory was shared between us and KKC on a 50/50 basis until April 2023. In April 2023, commercialization responsibilities for Crysvita in the Profit-Share Territory transitioned to KKC and KKC assumed responsibility for the commercialization of Crysvita in the Profit-Share Territory at and after April 2023. Thereafter, we are entitled to receive a tiered double-digit revenue share from the mid-20% range up to a maximum rate of 30%, intended to approximate the profit-share. Our and KKC’s obligations to pay royalties will continue on a country-by-country basis for so long as we or KKC, as applicable, are selling products in such country.

In 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.

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 Europe and 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.

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.

Regeneron

In January 2022, we announced a collaboration with Regeneron to commercialize Evkeeza for HoFH outside of the U.S. 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. The Company paid Regeneron a $30.0 million upfront payment. To date, we have recognized an aggregate of $27.5 million for regulatory and sales milestones and have in aggregate up to $35.5 million of future obligations for additional regulatory and sales milestones, if achieved. We may share in certain costs for global trials led by Regeneron and also received the right to opt into other potential indications.

Under the collaboration agreement, Regeneron supplies the product and charges us a transfer price from the low 20% range up to 40% of net sales.

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 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.

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.

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.

University of Pennsylvania

In May 2016, we entered into a research, collaboration and license agreement with the University of Pennsylvania, or UPENN, 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 a Program Agreement and a Unitholder Option Agreement with GeneTx to collaborate on the development of GeneTx's GTX-102, an ASO for the treatment of Angelman syndrome. In July 2022, pursuant to the terms of the Unitholder Option Agreement, as amended, we exercised the 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 paid the option exercise price of $75.0 million, 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. During the year ended December 31, 2024, we achieved a $30.0 million regulatory milestone upon the initiation of the Phase 3 *Aspire* clinical study for GTX-102. In addition, we are obligated to pay 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, contingent upon the achievement of the milestones. We will also 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 unitholders are 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.

As part of our acquisition of GeneTx, we assumed a License Agreement with Texas A&M University, or TAMU. To date, we have recognized an aggregate of $0.5 million for clinical milestones under the TAMU agreement, and have in aggregate up to $23.0 million of future obligations for various future milestones, if achieved, a nominal annual license fee that may increase up to a maximum of $2.0 million, as well as royalties in the mid-single-digits of net sales.

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 EEA, UK, 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. To date we have recognized an aggregate $9.0 million for regulatory milestones and have in aggregate up to $245.0 million of future obligations for additional regulatory and sales milestones under the agreement, if achieved. 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. If we receive and resell an FDA PRV in connection with a new drug application approval, Mereo is entitled to receive a portion of proceeds from the sale of the PRV or a cash payment from us, in the event we choose to retain the PRV.

In December 2024, we entered into a manufacturing and supply agreement with Mereo where we are responsible for the supply of setrusumab to Mereo in the Mereo territory. Mereo is responsible to reimburse us for a portion of the manufacturing process development costs as well as future commercial supply costs.

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.

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 PCLTM 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 521,719 shares (as adjusted for the October 2022 reverse stock split) of Solid's common stock for an aggregate price of $40.0 million.

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, 2024, we own, jointly own, or have exclusive rights to more than 275 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 50 in-force patents issued by the U.S. Patent and Trademark Office, or the USPTO. Furthermore, as of December 31, 2024, we own, jointly own, or have exclusive rights to more than 325 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, 2024, are summarized below.

Crysvita 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 six 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 Exclusivity

We own four issued U.S. patents and 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.

Dojolvi Exclusivity

We have an exclusive license from BRI to patents and patent applications relating to Dojolvi and its use for the treatment of FAOD. Pursuant to this license, we have rights to two issued U.S. patents covering Dojolvi which expire in 2025 and 2029. Beyond the patent portfolio in-licensed from BRI, we own four pending U.S. patent applications, corresponding foreign patent applications, and issued patents in Australia, Brazil, Canada, Israel, Korea, Malaysia, Taiwan, and Thailand 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 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 and 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 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 an exclusive sub-license to a patent family that includes three 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; this patent family is owned by UPENN and sublicensed to us by REGENX.

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 two issued U.S. patents 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).

UX111 (Rebisufligene Etisparvovec) 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 (Antisense Oligonucleotide) Exclusivity

We have an exclusive license from 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. The in-licensed TAMU patent family includes four issued U.S. patents expiring in 2038 (not accounting for any available PTE). Beyond the patent estate licensed from TAMU, we own a pending patent family relating to dosing regimens for the use of UBE3A antisense oligonucleotides including

GTX-102 in the treatment of Angelman syndrome; we expect any patents emanating from this patent family to expire in 2045 (not accounting for any available PTE).

UX701 (Rivunatpagene Miziparvovec) Exclusivity

We have two licenses to patents and patent applications covering elements of our UX701 product candidate. First, we have a license to a U.S. patent expiring in January 2026 which relates to the AAV9 capsid used in UX701; this patent is owned by UPENN and sublicensed to us by REGENX. 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).

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

While we currently contract with third parties for the manufacturing and testing of most of our products and product candidates for use in preclinical, clinical, and commercial applications, 2024 was the first full year of Good Manufacturing Practices, or GMP, operation for our Gene Therapy Manufacturing Facility in Bedford, Massachusetts. This facility is focused on drug substance and drug product manufacturing of AAV gene therapy products and will support our clinical and commercial pipeline. This new capability combines with our existing gene therapy process and analytical development and QC lab capabilities in nearby Woburn, Massachusetts to form a fully integrated gene therapy development, manufacturing, and testing unit.

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.

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. 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.

Crysvita

The drug substance and drug product for burosumab are made by KKC in Japan under the collaboration and license agreement and supply agreements 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.

In March 2023, the Dojolvi drug product manufacturer Aenova Haupt Pharma Wolfratshausen GmbH notified us of their intent to close the facility by the end of 2023. In response to this information, we produced additional DP batches prior to the facility closure at the end of 2023 and have identified a new DP manufacturer. We have completed the process performance validation activities and plan to submit the regulatory change in early 2025. Our current DP inventories are expected to support demand through at least the end of 2025.

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 marketing, 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, specialty distributors, 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 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, or for BLA products, the safety, purity, and potency, 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 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.

Pursuant to Title 21 of the Code of Federal Regulations, the FDA conducts a preliminary review of an NDA within 60 days of receipt. FDA procedures provide that the FDA will inform the sponsor by the 74th day after the FDA's receipt of submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing, in which case the application must be resubmitted with the requested additional information. The resubmitted application is also subject to review before it is accepted for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

Once an NDA or BLA has been accepted, 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, assessment plans, 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. The FDA may require, as appropriate, that such studies be underway prior to approval or within a specific time period after the date of approval for a product that has been granted accelerated approval. The FDA also has authority for expedited procedures to withdraw approval of a product or indication that was initially approved under accelerated approval if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, as a condition for accelerated approval, the FDA currently also requires pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

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 to treat, modify, reverse, or cure a serious or life-threatening condition and preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such condition. Advantages of the RMAT designation include early interactions with the FDA to discuss the development plan for the product candidate, including potential surrogate or intermediate endpoints, and eligibility for rolling and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. RMAT-designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real-world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy.

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 must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are publicly disclosed by the FDA.

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 submitted 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 is 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 began in 2023. Effective from 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.

Section 505(b)(2) New Drug Applications

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant, and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional bridging studies or measurements, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new drug candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that a Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity (such as exclusivity for obtaining approval of a new chemical entity) listed in the Orange Book for the referenced product has expired and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit, or a decision in the infringement case that is favorable to the Section 505(b)(2) 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 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 or receiving renumeration in return for, and from knowingly and willfully offering or paying remuneration to induce, referrals of federal healthcare program patients and 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 to Medicare, Medicaid, or other third-party payers, claims for payment that are false or fraudulent;
- 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 to Medicare, Medicaid, or other third-party payers, claims for payment that are false or fraudulent;
- international data protection laws and regulations, including, but not limited, to the EU General Data Protection Regulation, or GDPR, which apply to processing of personal data in the context of the activities of an entity established in a respective country, and to processing by an entity not established in a particular country, but where such processing is related to the offering of goods or services to, or the monitoring of the behavior of individuals located therein, and imposes requirements and limitations relating to the processing, storage, purpose of collection, accuracy, security, sharing and transfer of personal data, in particular with respect to special categories of personal data like health data, and the notification of supervisory authorities about data breaches, accompanied by sanctioning mechanisms—in addition to the GDPR, EU member states may also impose additional requirements in relation to health, genetic and biometric data through their national implementing legislation;
- 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.

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 UK 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, 2024, 49% of our total revenues were generated by our collaboration partner KKC.

Human Capital

General Information

As of December 31, 2024, we had 1,294 total employees, of which 875 are in research and development and 419 are in sales, general, and administrative. Further, 1,081 employees are based in the U.S., including at our facilities in Novato, California, Brisbane, California, Cambridge, Massachusetts, and Woburn, Massachusetts, and 213 employees are based at our international locations. The majority of new employees hired during the year ended December 31, 2024 were to support and extend our clinical and preclinical pipeline, our in-house manufacturing capacities for our GTMF, 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 strategically add employees in 2025 with a focus on increasing our commercial expertise and bandwidth for anticipated new product launches 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. Our health and safety management system includes several elements, such as incorporation of Global Environmental, Health, Safety and Sustainability standards, site-specific standard operating procedures, incident and safety observation reporting, hazard identification and risk assessments, job safety analyses, ergonomic assessments and industrial hygiene evaluations. We have adopted a flexible, hybrid working arrangement for our employees, which allows some of our employees to work remotely during certain days of the week. We provide our employees with wellness offerings to support their physical and mental health including our “Caring For U” program, a global reimbursement program offering employees up to $1,200 annually (in local currency) for wellness and caregiving activities.

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 tailored for new leaders as well as for more senior leaders, six sigma certification, 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 offer on-demand career coaching services through an external network of professional executive coaches. We encourage all employees to have an individual development plan to identify focus areas for learning and growth.

To regularly 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.

Culture

We are committed to fostering a healthy, inclusive environment while nurturing a culture of belonging where all employees have equal opportunities. We strive to create an environment where everyone we work with, serve, and engage with feels valued, respected, and empowered.

We have included questions in our engagement survey to measure employee perception of our inclusive culture, with the results from such survey on inclusion included in our corporate goals. Our business units review data related to hiring, promotions, and retention on an ongoing basis in order to promote inclusivity while maintaining our commitment to equal employment opportunities through merit-based decisions.

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. Our compensation structure includes performance-based elements, with the goal of recognizing and rewarding exceptional performance. We regularly review our compensation policies and practices in an effort to identify and address any disparities or inequities.

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. Moreover, some of the factors, events and contingencies discussed below may have occurred in the past, but the disclosures below are not representations as to whether or not the factors, events or contingencies have occurred in the past, and instead reflect our beliefs and opinions as to the factors, events, or contingencies that could materially and adversely affect us in the future. 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 expect to continue to incur operating losses in the near term.
- We have limited experience in generating revenue from product sales.
- We may need to raise additional capital to fund our activities.
- Clinical drug development is a lengthy, complex, and expensive process with uncertain outcomes.
- We may experience delays in commercialization of our products and other 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 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 commercialization of Crysvita in certain major markets, including the U.S. and Canada, and for our supply of Crysvita in our 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.
- 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 products and product candidates or from generic versions of our small-molecule products 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 to patent laws in the U.S. and other jurisdictions 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 limited experience as a company operating our own 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 employees or consultants may engage in misconduct which could cause significant liability for us.

• If we are found to have promoted off-label uses for our products, we may become subject to significant liability from the FDA and other regulatory agencies.

• 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 expect to continue to incur operating losses in the near term.

Since inception, we have been engaged in substantial research and development and capital investments, and we have operated at an operating loss each year and expect to continue doing so in the near term. While we currently expect to achieve profitability for the year 2027, our expectations are based on a variety of assumptions, and actual results, including whether we achieve profitability on our expected timeline or at all, may materially differ from our expectations. Our operating results, including our ability to achieve profitability, 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 our manufacturing-related facilities and capabilities, particularly as we continue to increase operations at our GMP gene therapy manufacturing facility;

• 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 or grow 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.

Even if we do achieve profitability, we may not be able to sustain or increase such profitability on a quarterly or yearly basis. Our operating results 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 may need to raise additional capital to fund our activities. Such 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, 2024, our available cash, cash equivalents, and marketable debt securities were $745.0 million. We may need additional capital to continue to commercialize our products, and to develop, 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 systems in our GMP gene therapy manufacturing facility;
- the cost of operating and maintaining our gene therapy manufacturing facility;
- 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 changing interest rates and inflation. 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 Co., Ltd., or 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.

In addition, we purchase or enter into a variety of financial instruments and transactions, including investments in commercial paper, the extension of credit to corporations, institutions and governments. If any of the issuers or counterparties to these instruments were to default on their obligations, it could materially reduce the value of the transaction and adversely affect our cash flows.

If our cash flows are materially and adversely affected or if we are unable to access our existing cash, cash equivalents and investments and/or 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. 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 have also been required to, or have chosen 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, 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 inflation;

• 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. 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. 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 sales 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 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. 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 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, designations 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 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 PRV Voucher Program began to sunset on December 20, 2024 such that the FDA may only award a PRV for a product application if a company received the rare pediatric disease designation from the FDA for the product candidate by December 20, 2024 and the FDA will cease awarding PRVs after September 30, 2026. Renewal of the PRV Voucher Program is subject to approval by Congress and it is currently uncertain whether the program will be renewed and whether any such renewal will be retroactively effective. If the PRV program is not renewed by Congress and our qualifying product candidates are approved by the FDA after the deadline of September 30, 2026, 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 Phase 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;
- we may be required to change the way the product is administered;

- 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 there can be no assurance 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 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 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, disruption in utility services, human error or disruptions in the operations of our suppliers. Further, given that cGMP gene therapy manufacturing is a nascent industry, there are a small number of CMOs with the experience necessary to manufacture our gene therapy product candidates and we may have difficulty finding or maintaining relationships with such CMOs or hiring experts for internal manufacturing and accordingly, our production capacity may be limited.

Our gene therapy 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 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. Although we are not involved in the day-to-day operations of our contract manufacturers, we are ultimately responsible for ensuring that our products are manufactured in accordance with GMP regulations. 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. Due to the complexity of the processes used to manufacture our products and product candidates, we or any of our collaborators or contract manufacturers may be unable to comply with GMP regulations in a cost-effective manner and may be unable to initially or continue to pass a federal, national or international regulatory inspection. 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, warning or untitled letters, fines, unanticipated compliance expenses, 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, enforcement actions and criminal or civil prosecution. 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 critical reagents.

Companion diagnostics are subject to regulation by the 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 have also generated 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 could 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 commercialization of Crysvita in our markets, including the U.S. and Canada, and for our supply of Crysvita in our markets. Failure by KKC to commercialize Crysvita in those markets, or to supply Crysvita to us, could result in a material adverse effect on our business and operating results.

Pursuant to the terms of our collaboration and license agreement with KKC, or the collaboration agreement, commercialization responsibilities for Crysvita in the U.S. and Canada transitioned from us to KKC in April 2023. KKC also has the sole right to commercialize Crysvita in Europe and, at certain specified times, in Turkey, subject to certain rights retained. A substantial portion of our total revenue has been based on revenue from Crysvita, including royalty revenue we receive from KKC for sales of the product in the U.S. and Canada. The commercial success of Crysvita in territories in which KKC owns commercialization responsibilities, such as in the U.S. and Canada depends on, among other things, the efforts and allocation of resources of KKC in those territories, which we do not control. KKC has no obligation under the collaboration agreement to use diligent efforts to commercialize Crysvita in those territories. 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 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, 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 products and product candidates.

As we currently lack the resources and the full capability to manufacture all of our products and product candidates on a clinical or commercial scale, we rely on third parties to manufacture, store and distribute 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 the risk factor above entitled "- *Even if we obtain regulatory approval for our product candidates, our products remain subject to regulatory scrutiny*". 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 is 30% of net sales, 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, ceases operations, is acquired, enters into exclusive arrangements with a competitor 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 supply agreements and Regeneron pursuant to a supply agreement. Further, single source suppliers are also used for our gene therapy programs and for Dojolvi, for which we are in the process of qualifying our alternative supplier. We cannot provide assurances that qualifying alternate sources, if available at all, for any of our drug substances and drug products, and establishing relationships with such sources would not result in significant expense, supply disruptions 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. Furthermore, geopolitical tensions with China including the Congressional legislative proposal, titled the BIOSECURE Act, which would, among other things, prohibit U.S. federal funding in connection with biotechnology equipment or services produced or provided by Chinese biotechnology companies, and the recent requests by certain Congressional leaders that WuXi AppTech Co. and its affiliates be added to certain U.S. Government restricted entity lists, could lead to our competitors and other companies moving to suppliers outside of China, including to our current suppliers. Significant increases in business at our single source suppliers resulting from such activities could adversely limit capacity at such suppliers to manufacture our products or result in price increases, interruptions or delays of our products.

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 ultrarare 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 ultrarare genetic diseases. 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, including the use of artificial intelligence, or AI, 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 can often 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. Moreover, we also face increased competition from other companies that are using AI, some of whom may be able to more quickly and effectively identify and develop novel drug candidates compared to us and our business partners, which could impair our ability to compete effectively and have a material adverse effect on our business, results of operations, or financial condition.

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 expect to expand our commercial team in the United States as well as in Europe, Latin America and the Asia-Pacific region. This infrastructure consists of both office-based as well as field teams with technical expertise, and is expected to 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, 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 sales to sustain our business. We face competition from 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.

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 foreign markets, 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 U.S., 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 and Evkeeza based on current regulations, our estimate of pricing on approval of Dojolvi and Evkeeza 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 unsettled. 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 foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application or provide the basis for third parties to challenge the validity of an issued patent. 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, patent applications will issue, the breadth of any issued 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 from its earliest non-provisional 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 products or 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 law 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 inventions 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 remain unclear owing to the evolving nature of the law and the lengthy timelines associated with court system review and interpretation. Consequently, 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.

Outside the U.S., there have been changes to patent laws in certain jurisdictions that could impair our ability to obtain, maintain, or enforce our patents in those territories. For instance, Europe's new Unitary Patent system and Unified Patent Court, or the UPC, may present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. In 2012, as part of the European Patent Package, or the EU Patent Package, regulations were passed with the goal of providing a single pan-European Unitary Patent system and a new UPC, for litigation involving European patents. Implementation of the EU Patent Package occurred in June 2023. Under the UPC, all European patents, including those issued prior to ratification of the European Patent Package, will by default automatically fall under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum in which to seek central revocation of our European patents and allow for the possibility of a competitor to obtain pan-European injunctions. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. Under the EU Patent Package, we will have the right to opt our patents out of the UPC over the first seven years of the court's existence, but doing so may preclude us from realizing the benefits of the new unified court.

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 covers technology 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. Regarding our anti-sclerostin antibody product candidate, setrusumab, we are aware of litigation involving patents owned by a third-party, OssiFi-Mab LLC, or OMab, relating to methods of using sclerostin antagonists in combination with antiresorptive drugs to increase bone growth, bone formation, and/or bone density. Specifically, in the U.S., OMab has asserted certain patents expiring in 2027 or 2028 against Amgen based on Amgen's commercialization of an anti-sclerostin antibody, Evenity®, for the treatment of osteoporosis in postmenopausal women at high risk for fracture; Amgen denies infringement and asserts the OMab patents are invalid. In Europe, OMab was granted two patents with related subject matter; the first patent has been revoked while the second has been opposed by Amgen, UCB, and two anonymous parties. There is a risk that one or more 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 obtain 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. 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. Moreover, aspects of the law are still being evaluated and interpreted by courts. As a result, its ultimate impact, implementation and meaning are subject to uncertainty. Modification of the BPCI Act, or changes to the 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 small-molecule product such as Dojolvi. 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 innovator small-molecule product. 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.

During the year ended December 31, 2024, Navinta, Aurobindo, and Esjay filed ANDAs for generic versions of Dojolvi. We have filed a patent infringement suit under the Hatch-Waxman Act against Navinta, Aurobindo and Esjay in the United States District Court for the District of New Jersey in response to the notices. See "Item 3. Legal Proceedings" below for a description of our suit. We cannot predict the outcome of our suit, nor can we predict whether there will be additional ANDA filings for Dojolvi.

There have been a number of recent regulatory and legislative initiatives designed to encourage generic competition for small-molecule pharmaceutical products. For instance, in December 2019, the Creating and Restoring Equal Access to Equivalent Samples Act, or the CREATES Act, was enacted, which provides a legislatively defined private right of action under which eligible product developers can bring suit against companies who refuse to sell sufficient quantities of their branded products on commercially reasonable, market-based terms to support such eligible product developers' marketing applications. It is our policy to evaluate requests for samples of our branded products, and to provide samples in response to *bona fide*, CREATES Act-compliant requests from qualified third parties, including generic manufacturers.

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. For instance, if the existing ANDA filers or additional competitors are able to enter the market with generic versions of Dojolvi, our sales of Dojolvi could materially decline which could have an adverse impact on our financial results.

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.

If KKC, Regeneron, the University of Pennsylvania, REGENX, 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.

From time to time, we are involved in lawsuits to protect or enforce our patents or the patents of our licensors, or may 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 have in the past and may in the future 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. For example, in September 2024, we filed a patent infringement suit under the Hatch-Waxman Act against Navinta, Aurobindo and Esjay. See " – Legal Proceedings" below for more information regarding our suit. 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 to patent laws in the U.S. and other jurisdictions 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 recent years, the U.S. Supreme Court has ruled on several patent cases, and in some instances, narrowed the scope of patent protection available. In addition, there have been recent proposals for changes to U.S. laws that, if adopted, could impact our ability to obtain or maintain patent protection for our proprietary technologies. Depending on future actions by U.S. courts, U.S. Congress, the USPTO, and the relevant lawmaking bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents, shorten the term of our existing patents and patents that we might obtain in the future, or impair the validity or enforceability of our patents that may be asserted against our competitors or other third parties. Any of these outcomes could have a material adverse effect on our business.

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 limited experience as a company operating our own manufacturing facility and may experience unexpected costs or challenges.

Prior to construction of our Bedford, Massachusetts gene therapy manufacturing facility in 2023, we did not previously have experience as a company in operating our own manufacturing facility and at this point, we cannot assure that the facility will be fully utilized at all times. While our employees may be experienced in running a manufacturing facility, our limited experience as a company may contribute to unacceptable or inconsistent product quality success rates and yields, and we may be unable to maintain adequate quality control, quality assurance, and qualified personnel. We have incurred and will continue to incur significant expenses and costs to operate the facility, which may be subject to significant impairment if our gene therapy programs are unsuccessful. Before we can begin to commercially manufacture any of our product candidates at the facility, we must obtain regulatory approval from the FDA for our manufacturing processes and for the facility. In order to obtain approval, we will need to ensure that all of our processes, quality systems, methods, equipment, policies and procedures are compliant with cGMP. Until recently, few gene therapy products manufactured by a cGMP gene therapy manufacturing facility in the U.S. had received approval from the FDA; therefore, the time frame required for us to obtain such approval is uncertain. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to spend time, money and effort on production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

As we seek to optimize and operate our manufacturing process at the facility, we will likely face technical and scientific challenges, considerable capital costs and potential difficulty in recruiting and hiring experienced, qualified personnel at the facility which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. We may also experience unexpected technical, regulatory, safety, quality or operational issues during manufacturing campaigns. 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. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis 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. If another party obtains orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication, we may be precluded or delayed from commercializing the product in that indication.

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. Additionally, if a competitor obtains approval of the same drug for the same indication before us, and the FDA grants such orphan drug exclusivity, we would be prohibited from obtaining approval for our product for seven or more years, unless our product can be shown to be clinically superior.

Even though we have orphan drug designation for UX111, UX143, DTX301, DTX401 and UX701 in the U.S. and Europe and for GTX 102 in the U.S., 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.

We have recorded on our Consolidated Balance Sheets intangible assets for in-process research and development, or IPR&D, related to DTX301 and DTX401 as a result of the accounting for our acquisition of Dimension Therapeutics. We also recorded intangible assets related to our licenses for Dojolvi and 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 December 31, 2024.

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 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 evolving 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 less stringent than those 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 was previously the subject of review by applicable governmental authorities of compliance with various fraud and abuse laws. We settled the matter with the governmental authorities for an immaterial settlement amount and without any admission of legal liability. We cannot assure that our other operations or programs will not be subject to review by governmental authorities or 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, 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, including activities related to the build-out and operation of our gene therapy manufacturing facility, 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. An increasing portion of our revenues are based on our international operations, which exposes us to increased financial risks such as longer payment cycles, additional or more burdensome regulatory requirements of financial institutions outside of the U.S. and exposure to foreign currency exchange rate. We may implement currency hedges intended to reduce our exposure to changes in certain foreign currency exchange rates. However, our hedging strategies, if implemented, may not be successful, and any of our unhedged foreign exchange exposures will continue to be subject to market fluctuations. Further, we sell products in countries that face economic volatility and weakness. Although we have historically collected receivables from customers in those countries, continued weakness or additional deterioration of the local economies and currencies may cause customers in those countries to be unable to pay for our products. Additionally, if one or more of these countries were unable to purchase our products, our revenues would be adversely affected.

Doing business internationally involves a number of additional 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;
- export and import restrictions, including the impact from new or increased sanctions and tariffs, or threats or changes in policy with respect to sanctions or tariffs, that are contemplated or could be implemented by the current Presidential administration and by other countries against the U.S. in response;
- 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;
- natural disasters and geopolitical and economic instability, including wars, terrorism, political unrest (including, for example the conflict between Russia and Ukraine, the conflict between Israel and the surrounding areas, and the rising tensions between China and Taiwan), results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease, inflation, recession, 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 anti-corruption 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.

Our employees or consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee or consultant misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the EU Data Protection Directive. It is not always possible to identify and deter employee or consultant misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug products. In particular, a product may not be promoted in the U.S. for uses that are not approved by the FDA as reflected in the product's approved labeling or prior to regulatory approval. Further, any labeling approved by the FDA for our products or any of our product candidates may include restrictions on use, limit use to specific populations or include various other limitations. The FDA may impose further requirements or restrictions on the distribution or use of any of our other product candidates as part of a REMS plan. Physicians may nevertheless prescribe such products to their patients in a manner that is inconsistent with the approved label provided the company did not promote such use. If we are found to have promoted such off-label uses, we may become subject to significant liability. Similarly, the FDA strictly regulates the promotion of investigational products prior to approval, known as pre-approval promotion. The federal government has levied large civil and criminal fines and/or other penalties against companies for alleged improper promotion and has investigated and/or prosecuted several companies in relation to off-label and/or pre-approval promotion. The FDA has also requested that certain companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed, curtailed or prohibited or have delayed approval of investigational products due to pre-approval conduct. Inappropriate promotional activities may also subject a company to investigations, prosecutions and litigation by other government entities or private citizens

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. Cybersecurity incidents increasingly involve the use of AI and machine learning to launch more automated, targeted and coordinated attacks on targets. 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 and clinical data, and may experience similar incidents in the future. 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 hybrid working arrangements. Improper or inadvertent behavior by employees, contractors and others with permitted access to our systems, including through the use of generative AI technologies, 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. In addition, there can be no assurance that our insurance coverage will be sufficient to cover the financial, legal, business or reputational losses that may result from a cybersecurity incident. 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 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. We purchased 7,825,797 shares of common stock of Solid in October 2020. Our investment in Solid is being accounted for at fair value, as the fair value is readily determinable. 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, changing interest rates and inflation;

• 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 2023 Incentive Plan, as amended, or the 2023 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors, and consultants. At December 31, 2024, there were 6,139,766 shares available for future grants under the 2023 Plan.

Pursuant to our 2014 Employee Stock Purchase Plan, as amended, or the A&R ESPP, eligible employees can acquire shares of our common stock at a discount to the prevailing market price. At December 31, 2024, there were 6,409,256 shares available for issuance under the A&R ESPP.

Our board of directors has adopted an Employment Inducement Plan, which was amended in July 2024, or the Inducement Plan, with a maximum of 1,200,000 shares available for grant under the plan. At December 31, 2024, there were 211,628 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 2023 Plan, the A&R 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 bylaws; 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. For example, we have been defending a lawsuit filed in the U.S. District Court for the District of Maryland by the Estate of Henrietta Lacks alleging unjust enrichment arising from our receipt and use of HeLa cells. 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, as well as existing and proposed laws related to these topics, 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. Investors who are focused on ESG matters may seek enhanced ESG disclosures or to implement policies adverse to our business, and there can be no assurances that stockholders will not advocate, via proxy contests, media campaigns or other public or private means, for us to make corporate governance changes or engage in certain corporate actions. 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 culture 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 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 1C. Cybersecurity

In the ordinary course of our business, we collect, use, store, and transmit digitally large amounts of confidential, financial, sensitive, proprietary, personal, and health-related information. The secure maintenance of this information and our information technology systems is important to our operations and business strategy. To this end, we have implemented processes designed to assess, identify, and manage risks from potential unauthorized occurrences on or through our information technology systems that may result in adverse effects on the confidentiality, integrity, and availability of these systems and the data residing therein. Our cybersecurity program is informed in part by industry standards and best practices, such as the National Institute of Standards and Technology (NIST) Cybersecurity Framework. This program is managed and monitored by a dedicated information technology team, including a Senior Director of Information Security, and is led by our Senior Vice President, Chief Information Officer, or CIO. Our processes include mechanisms, controls, technologies, and systems designed to prevent or mitigate data loss, theft, misuse, or other security incidents or vulnerabilities affecting the data and maintain a stable information technology environment. Our program includes, for example:

- Regular penetration and vulnerability testing, data recovery testing, security audits, and ongoing risk assessments;
- Engagement of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security controls as part of our operational security model;
- Cybersecurity awareness training for our employees, contactors, incident response personnel, and senior management;
- A cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents and annual tabletop exercises with participants from cross functional teams;
- A third-party risk management process for service providers, suppliers, and vendors including due diligence prior to engagement and ongoing periodic review of our key technology vendors, and other contractors and suppliers.

Our CIO, together with our Senior Director of Information Security and other members of the IT leadership team, are responsible for assessing and managing cybersecurity risks. Our CIO has over ten years of experience managing information technology and cybersecurity. Our Senior Director of Information Security has over 25 years of experience managing information technology and cybersecurity matters and is certified as a Certified Information Systems Security Professional (CISSP). We consider cybersecurity, along with other significant risks that we face, within our overall enterprise risk management framework.

Since the beginning of the last fiscal year, we have not identified any risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected us , but we face certain ongoing cybersecurity risks or threats that, if realized, are reasonably likely to materially affect us. Additional information on cybersecurity risks we face is discussed in Part I, Item 1A, “Risk Factors,” under the heading “Our business and operations may be materially adversely affected in the event of computer system failures or security breaches.”

The Board of Directors, as a whole and at the committee level, has oversight for the most significant risks facing us and for our processes to identify, prioritize, assess, manage, and mitigate those risks. The Audit Committee, which is comprised solely of independent directors, has been designated by our Board to oversee cybersecurity risks. The Audit Committee receives regular updates on cybersecurity and information technology matters and related risk exposures from our CIO. The Board also receives updates from the Audit Committee on cybersecurity risks on a regular basis.

Item 2. *Properties*

Our primary operations are conducted at the leased facilities summarized in the below table. In 2023, we completed the construction of our gene therapy manufacturing facility located in Bedford, Massachusetts. 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 2026
Novato, California	Laboratory and office	October 2028
Brisbane, California	Office	June 2026
Somerville, Massachusetts	Laboratory and office	January 2030
Woburn, Massachusetts	Laboratory and office	April 2028
Woburn, Massachusetts	Laboratory and office	October 2026
Bedford, Massachusetts	Manufacturing facility	Owned property

Item 3. *Legal Proceedings*

Ultragenyx Pharmaceutical Inc. and Baylor Research Institute v. Navinta LLC, Aurobindo Pharma Limited, Aurobindo Pharma USA, Inc., Esjay Pharma Private Limited and Esjay Pharma LLC

On September 26, 2024, we filed a patent infringement suit under the Hatch-Waxman Act against Navinta, Aurobindo and Esjay in the United States District Court for the District of New Jersey. The suit is in response to notices from Navinta, Aurobindo, and Esjay concerning the filing of ANDAs with the FDA, seeking FDA approval to market a generic version of Dojolvi® (triheptanoin) along with Paragraph IV certifications which allege that one Orange Book-listed patent covering Dojolvi is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of the proposed generic product. The filing of the suit triggers a stay preventing the FDA from granting the ANDAs final approval, which stay extends to December 30, 2027 (i.e., the date that is seven and one-half years from the June 30, 2020 approval of Dojolvi). We intend to vigorously defend our intellectual property. In addition to the issued patents for Dojolvi listed in the Orange Book, we own a pending patent application relating to certain pharmaceutical compositions of triheptanoin, including Dojolvi, that would be expected to expire in 2034 upon an issuance. Dojolvi is also protected in the U.S. by regulatory exclusivity until 2025 and orphan drug exclusivity for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD) until 2027.

Aurobindo and Navinta answered the complaint on December 2, 2024 and December 30, 2024, respectively. Esjay filed a motion to dismiss the suit on December 2, 2024. We filed an opposition to Esjay's motion to dismiss on January 7, 2025.

Ultragenyx Pharmaceutical Inc. v. Catalent Maryland, Inc. and Catalent Pharma Solutions LLC

On October 9, 2024, we filed a suit against Catalent Maryland, Inc. and Catalent Pharma Solutions, LLC (collectively, Catalent) in the Superior Court of the State of Delaware alleging that Catalent fraudulently mispresented its manufacturing capabilities and serially breached the terms of its manufacturing agreement with us. Our suit seeks monetary damages from Catalent in excess of $100 million.

Catalent filed its response, which included a motion to dismiss the fraud claim alleged in the suit, on December 18, 2024. We filed an amended complaint in reply to Catalent's response on February 3, 2025.

Except as disclosed above, we are not currently a party to any other material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties or government regulators and, 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.

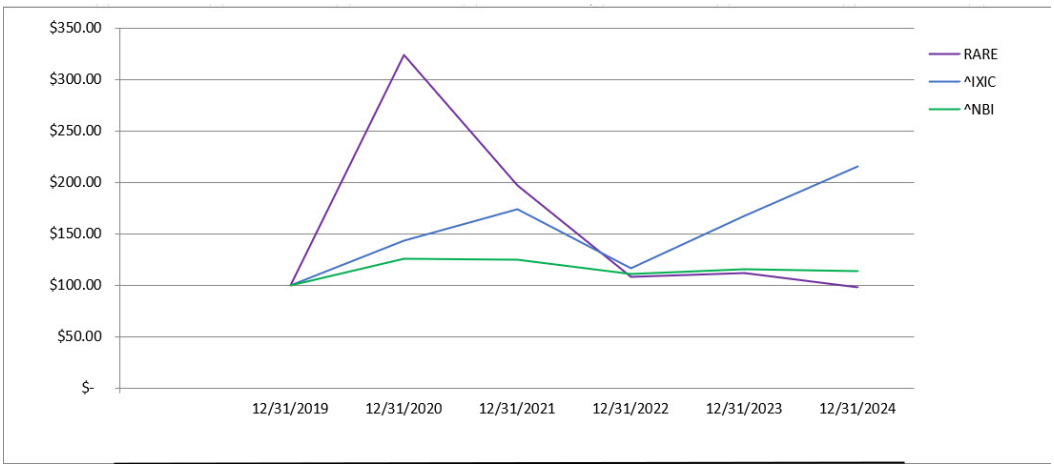
PART II

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, 2025, we had eight 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, 2019 through December 31, 2024. The figures represented below assume an investment of $100 in our common stock at the closing price of $42.71 on December 31, 2019 and in the Nasdaq Composite Index, or IXIC, and the Nasdaq Biotechnology Index, or NBI, on December 31, 2019 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, 2019	December 31, 2020	December 31, 2021	December 31, 2022	December 31, 2023	December 31, 2024
Ultragenyx Pharmaceutical Inc.	RARE	$ 100.00	$ 324.12	$ 196.89	$ 108.48	$ 111.96	$ 98.50
NASDAQ Composite Index	^IXIC	$ 100.00	$ 143.64	$ 174.36	$ 116.65	$ 167.30	$ 215.22
NASDAQ Biotechnology Index	^NBI	$ 100.00	$ 125.69	$ 124.89	$ 111.27	$ 115.42	$ 113.84

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, 2024, including year-over-year comparisons versus the year ended December 31, 2023. Our Annual Report on Form 10-K for the year ended December 31, 2023 includes a discussion and analysis of our financial condition and results of operations for the year ended December 31, 2022 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 committed to bringing novel products to patients for the treatment of serious rare and ultrarare genetic diseases. We have built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are typically no approved therapies treating the underlying disease. Our strategy is predicated upon time- and cost-efficient drug development, 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, AAV 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 $569.2 million and $606.6 million for the years ended December 31, 2024 and 2023, respectively. 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, 2024, our total revenues increased to $560.2 million, compared to $434.2 million for the same period in 2023. The increase in revenue was driven by higher demand for our approved products.

As of December 31, 2024, we had $745.0 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. Summary of Significant Accounting Policies" 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 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

Product Sales

We sell our approved products through a limited number of distributors. Under Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers*, revenue from product sales is recognized at the point in time when control is transferred 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, negotiated pricing, 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.

Collaboration, License and Royalty Revenue

We have certain license and collaboration agreements that are within the scope of 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.

We utilize certain information from our collaboration partners to record collaboration revenue, 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*, 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 recognize revenue by measuring the progress towards complete satisfaction of the performance obligations using input measures.

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 approval of our products by the U.S. Food and Drug Administration, or FDA, manufacturing and related costs are expensed. As of December 31, 2024, 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 European Union, or the EU, the UK, and Switzerland, effective January 1, 2020, under the terms of our Collaboration and License Agreement with Kyowa Kirin Co., Ltd., or 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

is based on net sales of Crysvita beginning in April 2023 and continuing until expiration, which is 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.

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. Our effective annual interest rates were 6.2% and 7.5%, for RPI and OMERS, respectively, as of December 31, 2024.

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, 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. 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, 2024, 2023, and 2022, stock-based compensation expense was $158.1 million, $135.2 million, and $130.4 million, respectively. As of December 31, 2024, we had $256.8 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 2 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.

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, 2024, our total gross deferred tax assets were $1,213.7 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, 2024 and 2023

Revenues (dollars in thousands)

	Year Ended December 31, 2024	2023	Dollar Change	Percent Change
Product sales:				
Crysvita	$ 134,709	$ 75,697	$ 59,012	78%
Dojolvi	88,194	70,633	17,561	25%
Evkeeza	32,162	3,642	28,520	*
Mepsevii	30,350	30,441	(91)	0%
Total product sales	285,415	180,413	105,002	58%
Crysvita royalty revenue	274,815	182,652	92,163	50%
Collaboration and license revenue:				
Crysvita collaboration revenue in Profit-Share Territory	—	69,705	(69,705)	*
Other	—	1,479	(1,479)	*
Total collaboration and license revenue	—	71,184	(71,184)	*
Total revenues	$ 560,230	$ 434,249	$ 125,981	29%

* not meaningful

Our product sales increased $105.0 million for the year ended December 31, 2024, compared to the same period in 2023. The increase was primarily due to an increase in demand for Crysvita in Latin America resulting from an increase in the number of patients on therapy, ongoing launch of Evkeeza in Japan and in Europe, Middle East and Africa territories, or EMEA, and continued increase in demand for our other approved products.

Our Crysvita royalty revenue and collaboration revenue in the Profit-Share Territory increased by a net $22.5 million for the year ended December 31, 2024, compared to the same period in 2023; this increase in Crysvita revenue is primarily due to an increase in the number of patients on therapy. We transitioned commercial responsibilities to KKC in the Profit-Share Territory in April 2023. Post transition, we recognize our revenue share for Crysvita sales in the Profit-Share Territory as royalty revenue, which was recorded as collaboration revenue prior to the transition.

Other revenue decreased by $1.5 million for the year ended December 31, 2024, compared to the same period in 2023. The decrease was due to the completion of the technology transfer and the technology transfer period related to the Daiichi Sankyo agreement as of March 31, 2023.

Cost of Sales (dollars in thousands)

	Year Ended December 31, 2024	2023	Dollar Change	Percent Change
Cost of sales	$ 76,728	$ 45,209	$ 31,519	70%

Cost of sales increased by $31.5 million for the year ended December 31, 2024, compared to the same period in 2023. The increase in cost of sales was due to an increase in demand for our approved products, primarily Crysvita in Latin America and Evkeeza in EMEA and Japan.

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 and at our gene therapy manufacturing facility, 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.

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. Approved products include costs for disease monitoring programs for post-marketing clinical studies, medical affairs activities to support scientific discovery efforts on existing programs, and regulatory costs for unapproved regions. Infrastructure costs include direct costs related to laboratory, IT, and equipment depreciation costs, and overhead allocations for human resources, IT, and other allocable costs.

We manage our research and development expenses by identifying the research and development activities we expect to be performed during a given period and then prioritizing efforts based on anticipated probability of successful technical development and regulatory approval, market potential, available human and capital resources, scientific data and other considerations. We regularly review our research and development activities based on unmet medical need and, as necessary, reallocate resources among our research and development portfolio that we believe will best support the long-term growth of our business. We allocate and analyze certain operational expenses by individual product candidates, specifically costs to conduct clinical studies, including expenses incurred with clinical research organizations, direct manufacturing costs, and salaries and benefits. Other operational expenses are not allocated and analyzed by individual product candidates. For instance, costs associated with Chemistry, Manufacturing and Controls, or CMC costs, are primarily purchases of materials for our internal gene therapy manufacturing activities that qualify as research and development expenses at the time of purchase but for which the allocation and consumption of such costs by a specific product candidate is not determined; accordingly, CMC costs for gene therapy programs are generally spread across multiple product candidates. Although we do track and allocate certain operational R&D costs at the individual product candidate level, as described above and as reflected in the table below, we do not fully track and allocate research and development expenses at the individual product candidate level.

The following table provides a breakout of our research and development expenses by individual product candidate under each major clinical program type and other research and development categories:

	Year Ended December 31, 2024	2023	Dollar Change	Percent Change
Clinical programs:				
Gene therapy programs				
DTX301	$ 40,831	$ 31,439	$ 9,392	30%
DTX401	75,340	72,103	3,237	4%
UX701	33,207	24,079	9,128	38%
UX111	41,323	24,412	16,911	69%
CMC costs	3,459	16,672	(13,213)	-79%
Total gene therapy programs	194,160	168,705	25,455	15%
Biologic and nucleic acid programs				
GTX102	50,757	31,121	19,636	63%
UX053	374	12,821	(12,447)	-97%
UX143	89,118	64,972	24,146	37%
Total biologic and nucleic acid programs	140,249	108,914	31,335	29%
Translational research	45,702	71,820	(26,118)	-36%
Upfront license, acquisition, and milestone fees	30,450	9,000	21,450	238%
Approved products	35,432	53,478	(18,046)	-34%
Infrastructure	81,034	78,929	2,105	3%
Stock-based compensation	86,616	74,531	12,085	16%
Other research and development	84,222	83,072	1,150	1%
Total research and development expenses	$ 697,865	$ 648,449	$ 49,416	8%

Total research and development expenses increased $49.4 million for the year ended December 31, 2024 compared to the same period in 2023. The change in research and development expenses was due to:

- for gene therapy programs, an increase of $25.5 million, primarily related to BLA filing activities for UX111, and continued clinical progress of the other programs, combined with the transition of certain programs to in-house manufacturing which resulted in a decrease in CMC costs and an increase in internal manufacturing costs;
- for biologic and nucleic acid programs, an increase of $31.3 million, primarily related to the continued clinical progress of the UX143 and GTX102 programs and associated clinical development and manufacturing expenses, partially offset by a reduction in development expense on UX053 for the treatment of Glycogen Storage Disease Type III due to cessation of development activities for the program;
- for translational research, a decrease of $26.1 million, primarily related to decreases in manufacturing and headcount expense for early stage and IND-stage projects;
- for upfront license, acquisition, and milestone fees, an increase of $21.5 million, primarily related to the achievement of a clinical enrollment milestone on the GTX-102 program during 2024;
- for approved products, a decrease of $18.0 million, primarily due to reduced reimbursement of Regeneron collaboration expenses with the completion of the pediatric and open label extension trials for Evkeeza and reduced operating expenses for Crysvita post-marketing studies;
- for infrastructure, an increase of $2.1 million, primarily related to depreciation of the gene therapy manufacturing facility, depreciation of laboratory-related leasehold improvements and equipment, and IT-related expenses;
- for stock-based compensation an increase of $12.1 million, primarily related to the increase in total value of stock-based awards granted to employees; and
- for other research and development expenses, an increase of $1.2 million, primarily related to increased staffing to support internal manufacturing, and 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, 2024	2023	Dollar Change	Percent Change
Selling, general and administrative	$ 321,610	$ 309,799	$ 11,811	4%

Selling, general and administrative expenses increased $11.8 million for the year ended December 31, 2024, compared to the same period in 2023.

We expect annual selling, general and administrative expenses to increase in the future as we continue to support our existing approved products, multiple clinical-stage product candidates, and planned launches of additional products.

Interest Income (dollars in thousands)

	Year Ended December 31, 2024	2023	Dollar Change	Percent Change
Interest income	$ 36,506	$ 26,688	$ 9,818	37%

Interest income increased $9.8 million for the year ended December 31, 2024 compared to the same period in 2023, primarily due to higher marketable debt securities balances.

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

	Year Ended December 31, 2024	2023	Dollar Change	Percent Change
Change in fair value of equity investments	$ (1,115)	$ 397	$ (1,512)	(381%)

For the years ended December 31, 2024 and 2023, we recorded a net decrease of $1.1 million and a net increase of $0.4 million, respectively, in the fair value of our equity investments due to unrealized loss and gain, respectively, on our investment in Solid Biosciences Inc., or Solid, common stock.

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

	Year Ended December 31, 2024	2023	Dollar Change	Percent Change
Non-cash interest expense on liabilities for sales of future royalties	$ 63,041	$ 66,004	$ (2,963)	(4%)

The non-cash interest expense on liabilities for sales of future royalties decreased by $3.0 million for the year ended December 31, 2024, compared to the same period in 2023, primarily due to a reduction in total royalty obligation balances as a result of increased royalties generated from our collaboration partner, KKC. To the extent the royalty payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, we prospectively adjust the effective interest rate.

Other Expense (dollars in thousands)

	Year Ended December 31, 2024	2023	Dollar Change	Percent Change
Other expense	$ (3,963)	$ (337)	$ (3,626)	*

Other expense increased $3.6 million for the year ended December 31, 2024, compared to the same period in 2023. These changes were primarily due to fluctuations in foreign exchange rates.

(Provision for) Benefit from Income Taxes (dollars in thousands)

	Year Ended December 31, 2024	2023	Dollar Change	Percent Change
(Provision for) benefit from income taxes	$ (1,597)	$ 1,825	$ (3,422)	(188%)

For the year ended December 31, 2024, we recognized an income tax provision of $1.6 million attributable to income tax expense of $0.2 million for state tax, and income tax expense of $1.4 million from foreign jurisdictions. For the year ended December 31, 2023, we recognized an income tax benefit of $4.8 million attributable to modifications in our state apportionment

methodology. We realized no benefit for 2023 losses due to a full valuation allowance against the U.S. net deferred tax assets. The benefit was offset by an income tax expense of $3.0 million from foreign jurisdictions.

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, 2024, we had $745.0 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 12 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, 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 June 2024, we completed an underwritten public offering in which 8,782,051 shares of common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional 1,346,153 shares, at a public offering price of $39.00 per share. In connection with the offering, we sold to certain investors pre-funded warrants, in lieu of common stock, to purchase 1,538,501 shares of common stock at a purchase price of $38.999 per pre-funded warrant, which equals the public offering price per share of common stock less the $0.001 exercise price per share of each pre-funded warrant. The total proceeds that we received from the offering were $381.0 million, net of underwriting discounts and commissions.

As of December 31, 2024, none of the pre-funded warrants had been exercised.

In February 2024, we entered into a Sales Agreement with Cowen and Company, LLC, or Cowen, 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 Cowen. No shares were sold under this agreement during the year ended December 31, 2024.

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

	Year Ended December 31,	
	2024	2023
Cash used in operating activities	$ (414,188)	$ (474,806)
Cash (used in) provided by investing activities	(17,768)	168,000
Cash provided by financing activities	399,241	388,142
Effect of exchange rate changes on cash	(2,525)	462
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (35,240)	$ 81,798

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, 2024 was $414.2 million and primarily reflected a net loss of $569.2 million, partially offset by non-cash items of $141.1 million, net, which consisted primarily of non-cash collaboration royalty revenues, interest expense related to the sale of future royalties to RPI and OMERS, stock-based compensation, amortization of discounts on marketable debt securities, and depreciation and amortization. The change in operating assets and liabilities also reflected a net increase of cash of $13.9 million, primarily due to an increase in accounts payable, accrued, and other liabilities, primarily related to an increase in accrued collaboration and higher revenue reserves from increased sales of our approved products, combined with an increase in inventory, primarily for Mepsevii and Evkeeza, partially offset by a decrease in prepaid expenses and other assets, primarily in prepaid manufacturing.

Cash used in operating activities for the year ended December 31, 2023 was $474.8 million and primarily reflected a net loss of $606.6 million, partially offset by non-cash items of $146.9 million, net, which consisted primarily of non-cash collaboration royalty revenues, interest expense related to the sale of future royalties to RPI and OMERS, net of amounts capitalized, stock-based compensation, amortization of discounts on marketable debt securities, and depreciation and amortization. The change in operating assets and liabilities also reflected a net use of cash of $15.1 million, primarily due to an increase in accounts receivable primarily related to an increase in sales of our approved products, partially offset by a net decrease in prepaid expenses and other assets, primarily in prepaid manufacturing.

Cash (Used in) Provided by Investing Activities

Cash used in investing activities for the year ended December 31, 2024 was $17.8 million and was primarily related to $12.5 million in payments for intangible assets related to milestones on our commercial products, partially offset by $4.7 million from net activities in marketable debt securities.

Cash provided by investing activities for the year ended December 31, 2023 was $168.0 million and was primarily related to $219.8 million from net activities in marketable debt securities, offset by purchases of property, plant, and equipment of $44.3 million, primarily related to the fit-out of our gene therapy manufacturing facility.

Cash Provided by Financing Activities

Cash provided by financing activities for the year ended December 31, 2024 was $399.2 million and was primarily comprised of $381.0 million in net proceeds from the sale of common stock in our June 2024 underwritten public offering and $11.3 million in proceeds from the issuance of common stock from exercise of warrants and equity plan awards, net.

Cash provided by financing activities for the year ended December 31, 2023 was $388.1 million and was primarily comprised of $326.5 million in net proceeds from the sale of common stock in our October 2023 underwritten public offering and $53.3 million in net proceeds from the issuance of common stock from our ATM.

Funding Requirements

We anticipate that, excluding non-recurring items, we will continue to generate annual losses in the near term as we continue the development of, and seek regulatory approvals for, our product candidates, and continue with commercialization of approved products. We may 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 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;
- the cost of operating our GMP gene therapy manufacturing facility;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory interactions and approvals;
- the cost and timing of establishing our commercial infrastructure, and distribution capabilities;
- the impact of macroeconomic conditions, including general economic slowdowns, changing interest rates and inflation on our business operations and operating results; 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 10. Leases" to the Consolidated Financial Statements for amounts outstanding for operating and finance leases as of December 31, 2024.

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 16. Commitments and Contingencies" 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 9. License and Research Agreements" to the Consolidated Financial Statements.

Recent Accounting Pronouncements

In November 2024, the FASB issued ASU 2024-03, *Income Statement-Reporting Comprehensive Income-Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses*, requiring public entities to disclose additional information about specific expense categories in the notes to the financial statements on an interim and annual basis. ASU 2024-03 is effective for fiscal years beginning after December 15, 2026, and for interim periods beginning after December 15, 2027, with early adoption permitted. We are currently evaluating the impact of adopting ASU 2024-03.

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, requiring public entities to disclose information about their reportable segments’ significant expenses and other segment items on an interim and annual basis. Public entities with a single reportable segment are required to apply the disclosure requirements in ASU 2023-07, as well as all existing segment disclosures and reconciliation requirements in ASC 280 on an interim and annual basis. We adopted ASU 2023-07 during the year ended December 31, 2024.

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, 2024, we had cash, cash equivalents, and marketable debt securities totaling $745.0 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, 2024. To date, we have not experienced a loss of principal on any of our investments and as of December 31, 2024, 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 macroeconomic environment (including financial conditions affecting the banking system and financial institutions), 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, 2024, 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 our 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. In connection with that evaluation, our Principal Executive Officer and our 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, 2024. 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 our 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, 2024, 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, 2024, 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, 2024, 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, 2024, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2024 and 2023, 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, 2024, and the related notes and our report dated February 19, 2025 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 19, 2025

Item 9B. *Other Information*

During the three months ended December 31, 2024, the following directors and officers adopted a Rule 10b5-1 trading arrangement intended to satisfy the affirmative defense conditions of Rule 10b5-1(c).

Name and Title	Date	Aggregate Number of Shares of Common Stock to be Sold (Subject to Certain Conditions)	Plan End Date
	Adopted		
Shehnaaz Suliman, M.D., Ph.D. Board Member	November 8, 2024	Up to 27,110 shares, all of which are shares to be acquired upon the exercise of stock options	November 7, 2025
Corsee Sanders, Ph.D., Board Member	November 15, 2024	Up to 2,405 shares	June 26, 2025
Matthew Fust, Board Member	November 22, 2024	Up to 15,000 shares, all of which are shares to be acquired upon the exercise of stock options	November 21, 2025
Eric Crombez, M.D. EVP, Chief Medical Officer	December 3, 2024	Up to 64,235 shares, 28,500 of which are shares to be acquired upon the exercise of stock options	December 3, 2025
Howard Horn, EVP, Chief Financial Officer	December 9, 2024	Up to 17,477 shares	December 9, 2025

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 2025 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 "2025 Proxy Statement", including under the headings "Nominees and Incumbent Directors," "Executive Officers," ""Board of Directors and Committees," "Corporate Governance" and, as applicable, "Delinquent Section 16(a) Beneficial Ownership Reports." We have adopted a Global Code of Conduct that applies to all of our directors, officers and employees, including our principal executive, principal financial and principal accounting officers, or persons performing similar functions. Our Global Code of Conduct 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 Global Code of Conduct, and waivers of the Global Code of Conduct 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 2025 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 2025 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 2025 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 2025 Proxy Statement, including under the heading "Proposal No. 3—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	Second Amended and Restated Bylaws	8-K	12/21/2023	3.1	
4.1	Form of Common Stock Certificate	S-1	11/8/2013	4.2	
4.2	Form of Indenture	S-3 ASR	2/21/2024	4.2	
4.3	Form of Pre-Funded Warrant	8-K	10/23/2023	4.1	
4.4	Form of Pre-Funded Warrant	8-K	6/17/2024	4.1	
4.5	Description of Common Stock	10-K	2/14/2020	4.3	
10.1*	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	
10.2	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	
10.3	Amendment No. 2 to Collaboration and License Agreement, effective as of November 28, 2016, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.3	
10.4*	Amendment No. 3 to Collaboration and License Agreement, effective September 29, 2017, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.4	
10.5*	Amendment No. 4 to Collaboration and License Agreement, effective as of January 29, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-K	2/21/2018	10.5	
10.6*	Amendment No. 5 to Collaboration and License Agreement, effective as of April 30, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	8/3/2018	10.1	
10.7*	Amendment No. 6 to Collaboration and License Agreement, effective as of February 1, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	5/7/2019	10.2	

10.8*	Amendment No. 7 to Collaboration and License Agreement, effective as of December 5, 2018, between Ultragenyx Pharmaceutical Inc. and Kyowa Hakko Kirin Co., Ltd.	10-Q	5/7/2019	10.3	
10.9*	Amendment No. 8 to Collaboration and License Agreement, effective as of July 4, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. (formerly, Kyowa Hakko Kirin Co., Ltd.)	10-Q	8/2/2019	10.1	
10.10*	Amendment No. 9 to Collaboration and License Agreement, effective December 23, 2019, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd.	10-K	2/14/2020	10.10	
10.11*	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	
10.12*	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	
10.13*	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	
10.14*	Amendment No. 13 to Collaboration and License Agreement, effective as of May 16, 2023, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Co., Ltd.	10-Q	8/3/2023	10.1	
10.15*	Supply Agreement, effective as of November 18, 2020, between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin Inc.				X
10.16*	Amendment No. 1, effective as of September 13, 2024, to the Supply Agreement between Ultragenyx Pharmaceutical Inc. and Kyowa Kirin, Inc.				X
10.17*	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	
10.18*	Royalty Purchase Agreement, dated as of December 17, 2019, between Ultragenyx Pharmaceutical Inc. and RPI Finance Trust	10-K	2/14/2020	10.25	
10.19*	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	
10.20#	2014 Incentive Plan (as amended)	10-K	2/17/2017	10.20	
10.21#	Form of Incentive Stock Option Agreement (2014 Plan)	S-1/A	1/17/2014	10.14	
10.22#	Form of Non Statutory Stock Option Agreement (Employees) (2014 Plan)	S-1/A	1/17/2014	10.15	
10.23#	Form of Restricted Stock Unit Agreement (Employees) (2014 Plan)	10-Q	5/10/2016	10.1	
10.24#	Form of Non-Statutory Stock Option Agreement (Annual Grant for Directors) (2014 Plan)	10-Q	8/3/2021	10.2	
10.25#	Form of Restricted Stock Unit Agreement (Annual Grant for Directors) (2014 Plan)	10-Q	8/3/2021	10.3	

10.26#	Form of Non-Statutory Stock Option Agreement (Grant for New Directors) (2014 Plan)	10-Q	8/3/2021	10.4	
10.27#	Form of Restricted Stock Unit Agreement (Grant for New Directors) (2014 Plan)	10-Q	8/3/2021	10.5	
10.28#	Amended and Restated 2023 Incentive Plan	S-8	7/12/2024	4.4	
10.29#	Form of Incentive Stock Option Agreement (2023 Plan)	10-K	2/21/2024	10.30	
10.30#	Form of Non Statutory Stock Option Agreement (Employees)(2023 Plan)	10-K	2/21/2024	10.31	
10.31#	Form of Restricted Stock Unit Agreement (Employees) (2023 Plan)	10-K	2/21/2024	10.32	
10.32#	Form of Non-Statutory Stock Option Agreement (Annual Grant for Directors) (2023 Plan)	10-K	2/21/2024	10.33	
10.33#	Form of Restricted Stock Unit Agreement (Annual Grant for Directors) (2023 Plan)	10-K	2/21/2024	10.34	
10.34#	Form of Non-Statutory Stock Option Agreement (Grant for New Directors) (2023 Plan)	10-K	2/21/2024	10.35	
10.35#	Form of Restricted Stock Unit Agreement (Grant for New Directors) (2023 Plan)	10-K	2/21/2024	10.36	
10.36#	Form of Performance Stock Unit Agreement (2022)	10-Q	5/6/2022	10.1	
10.37#	Form of Performance Stock Unit Agreement (2023)	10-Q	5/4/2023	10.1	
10.38#	Form of Performance Stock Unit Agreement (2024)				X
10.39#	Amended and Restated 2014 Employee Stock Purchase Plan	S-8	6/8/2023	4.5	
10.40#	Corporate Bonus Plan	S-1/A	1/17/2014	10.27	
10.41#	Employment Inducement Plan	10-K	2/12/2021	10.43	
10.42#	First Amendment to Employment Inducement Plan	S-8	6/8/2023	4.7	
10.43#	Second Amendment to Employment Inducement Plan	S-8	7/12/2024	4.7	
10.44#	Form of Non Statutory Stock Option Agreement (Inducement Plan)	10-K	2/12/2021	10.44	
10.45#	Form of Non Statutory Stock Option Agreement (Inducement Plan) (ex-US)	10-K	2/12/2021	10.45	
10.46#	Form of Restricted Stock Unit Agreement (Inducement Plan)	10-K	2/12/2021	10.46	
10.47#	Form of Restricted Stock Unit Agreement (Inducement Plan)(ex-US)	10-K	2/12/2021	10.47	
10.48#	Ultragenyx Pharmaceutical Inc. Deferred Compensation Plan	10-Q	8/3/2021	10.1	
10.49#	Amendment No. 1 to the Ultragenyx Pharmaceutical Inc. Deferred Compensation Plan	10-Q	11/3/2021	10.1	
10.50#	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	
10.51#	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	

10.52#	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
10.53#	Offer Letter, dated as of October 31, 2011, between Ultragenyx Pharmaceutical Inc. and Thomas Kassberg	S-1	11/8/2013	10.19
10.54#	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
10.55#	Amendment No. 2, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Thomas Kassberg	10-Q	11/3/2022	10.5
10.56#	Offer Letter, dated as of April 26, 2016, between Ultragenyx Pharmaceutical Inc. and Karah Parschauer	10-Q	8/9/2016	10.3
10.57#	Amendment, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Karah Parschauer	10-Q	11/3/2022	10.6
10.58#	Offer Letter, dated as of February 20, 2015, between Ultragenyx Pharmaceutical Inc. and Dennis Huang	10-K	2/17/2017	10.36
10.59#	Amendment, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Dennis Huang	10-Q	11/3/2022	10.7
10.60#	Offer Letter, dated as of June 11, 2015, between Ultragenyx Pharmaceutical Inc. and John R. Pinion II	10-K	2/17/2017	10.37
10.61#	Amendment, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and John R. Pinion II	10-Q	11/3/2022	10.9
10.62#	Amended and Restated Offer Letter, dated March 31, 2023, between Ultragenyx Pharmaceutical Inc. and Eric Crombez, M.D.	10-Q	5/4/2023	10.2
10.63#	Offer Letter, dated June 2, 2023, between Ultragenyx Pharmaceutical Inc. and Howard Horn	8-K	7/12/2023	10.1
10.64#	Amendment, dated September 6, 2023, to the Offer Letter between Ultragenyx Pharmaceutical Inc. and Howard Horn	8-K	9/8/2023	10.1
10.65#	Offer Letter, dated May 16, 2017, between Ultragenyx Pharmaceutical Inc. and Erik Harris	10-Q	8/2/2019	10.4
10.66#	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
10.67#	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
10.68#	Amendment No. 3, dated September 13, 2022, to Offer Letter between Ultragenyx Pharmaceutical Inc. and Erik Harris	10-Q	11/3/2022	10.8
10.69#	Form of Indemnification Agreement	10-K	3/24/2014	10.23
10.70	Standard Lease, dated as of July 5, 2011, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.	S-1	11/8/2013	10.22

10.71	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	
10.72	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	
10.73	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	
10.74	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	
10.75	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	
10.76	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	
10.77	Addendum #7 to Standard Lease, effective as of November 22, 2024, between Ultragenyx Pharmaceutical Inc. and Condiotti Enterprises, Inc.				X
10.78	Lease Agreement, dated as of December 8, 2015, between Marina Boulevard Property, LLC and Ultragenyx Pharmaceutical Inc.	10-K	2/26/2016	10.43	
10.79	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	
10.80	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	
10.81	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	
10.82	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	
10.83	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	
10.84	Fifth Amendment, dated November 25, 2024, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No. 20, LLC				X
10.85	Lease Agreement, dated December 15, 2019, between Ultragenyx Pharmaceutical Inc. and ARE-San Francisco No. 17, LLC.	10-K	2/12/2021	10.81	
10.86	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	

10.87	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	
10.88	Third Amendment, dated July 27, 2022, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and ARE-San Francisco No. 17, LLC	10-K	2/16/2023	10.92	
10.89	Fourth Amendment, dated December 13, 2024, to the Lease Agreement between Ultragenyx Pharmaceutical Inc. and GI ETS Shoreline LLC (as successor-in-interest to ARE-San Francisco No. 17, LLC)				X
10.90	Office Lease, dated April 19, 2019, between Ultragenyx Pharmaceutical Inc. and Woburn MCB II, LLC	10-K	2/14/2020	10.70	
10.91	Commercial Lease, dated July 2, 2018, between Ultragenyx Pharmaceutical Inc. and 32 Leveroni LLC	10-K	2/14/2020	10.71	
10.92	Lease, dated August 18, 2022, between Ultragenyx Pharmaceutical Inc. and Brickbottom I QOZB L.P.	10-K	2/17/2023	10.95	
10.93	First Amendment, dated March 12, 2024, between Ultragenyx Pharmaceutical Inc. and Brickbottom I QOZB L.P.				X
19.1	Ultragenyx Insider Trading Policy				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 of Ultragenyx Pharmaceutical Inc., as required by Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X
31.2	Certification of 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
97.1	Ultragenyx Pharmaceutical Inc. Clawback Policy		2/21/2024	97.1	
101.INS	XBRL Instance Document, formatted in Inline XBRL				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document				X
104	The cover page from this Annual Report on Form 10-K, formatted in Inline XBRL and contained in Exhibit 101				X

* 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)

Date: February 19, 2025

POWER OF ATTORNEY

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

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

Signature	Title	Date
/s/ Emil D. Kakkis Emil D. Kakkis, M.D., Ph.D.	President and Chief Executive Officer and Director (Principal Executive Officer)	February 19, 2025
/s/ Howard Horn Howard Horn	Executive Vice President, Chief Financial Officer, Corporate Strategy (Principal Financial Officer)	February 19, 2025
/s/ Theodore A. Huizenga Theodore A. Huizenga	Senior Vice President and Chief Accounting Officer (Principal Accounting Officer)	February 19, 2025
/s/ Daniel G. Welch Daniel G. Welch	Chairman of the Board	February 19, 2025
/s/ Deborah Dunsire Deborah Dunsire, M.D.	Director	February 19, 2025
/s/ Matthew K. Fust Matthew K. Fust	Director	February 19, 2025
/s/ Michael Narachi Michael Narachi	Director	February 19, 2025
/s/ Amrit Ray Amrit Ray, M.D.	Director	February 19, 2025
/s/ Corsee D. Sanders Corsee D. Sanders, Ph.D.	Director	February 19, 2025
/s/ Shehnaaz Suliman Shehnaaz Suliman, M.D.	Director	February 19, 2025

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, 2024 and 2023, 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, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, 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, 2024, 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 19, 2025 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 account or disclosure to which it relates.

Liabilities for sales of future royalties

Description of the Matter	As discussed in Note 11, 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. 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	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.

in Our Audit

To test management's estimates of the future royalties and the amount of imputed effective interest rates, we performed audit procedures that included, among others, evaluating the reasonableness of management's assumptions related to the forecasted revenue growth rates, including 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 2012.

San Mateo, California
February 19, 2025

ULTRAGENYX PHARMACEUTICAL INC.

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

	December 31, 2024	December 31, 2023
ASSETS		
Current assets:		
Cash and cash equivalents[1]	$ 173,729	$ 213,584
Marketable debt securities	436,296	363,625
Accounts receivable, net	121,801	73,390
Inventory	45,007	33,969
Prepaid expenses and other assets	40,290	47,616
Total current assets	817,123	732,184
Property, plant, and equipment, net	265,929	290,566
Marketable debt securities	135,004	199,901
Intangible assets, net	178,314	166,271
Goodwill	44,406	44,406
Other assets	62,680	57,685
Total assets	$ 1,503,456	$ 1,491,013
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 38,756	$ 42,114
Accrued liabilities	240,973	196,486
Lease liabilities	10,297	12,595
Liabilities for sales of future royalties	49,847	29,242
Other liabilities	4,280	—
Total current liabilities	344,153	280,437

Lease liabilities	30,042	30,574
Deferred tax liabilities	30,058	30,058
Liabilities for sales of future royalties	819,824	862,325
Other liabilities	17,082	12,205
Total liabilities	1,241,159	1,215,599
Commitments and contingencies (Note 16)		
Noncontrolling interest	7,000	—
Stockholders' equity:		
Preferred stock, par value of $ 0.001 per share— 25,000,000 shares authorized; nil outstanding in 2024 and in 2023	—	—
Common stock, par value of $ 0.001 per share— 250,000,000 shares authorized; outstanding— 92,484,330 in 2024 and 82,315,590 in 2023	92	82
Treasury stock, at cost, 69,757 in 2024 and 9,559 in 2023	(3,593)	(432)
	3,593	432
Deferred compensation obligation		
Additional paid-in capital	4,212,692	3,662,346
Accumulated other comprehensive (loss) income	(643)	647
Accumulated deficit	(3,956,844)	(3,387,661)

Total stockholders' equity	255,297	275,414
Total liabilities, noncontrolling interest and stockholders' equity	$ 1,503,456	$ 1,491,013

See accompanying notes.

(1) The Company's Consolidated Balance Sheet as of December 31, 2024 includes $

13.5

million in cash and cash equivalents that can be used only to settle obligations of the consolidated variable interest entity. See "Note 7. Investment in Amlogenyx Inc."

ULTRAGENYX PHARMACEUTICAL INC.

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

	Year Ended December 31,		
	2024	2023	2022
Revenues:			
Product sales	$ 285,415	$ 180,413	$ 118,927
Royalty revenue	274,815	182,652	21,692
Collaboration and license	—	71,184	222,710
Total revenues	560,230	434,249	363,329
Operating expenses:			
Cost of sales	76,728	45,209	28,320
Research and development	697,865	648,449	705,789
Selling, general and administrative	321,610	309,799	278,139
Total operating expenses	1,096,203	1,003,457	1,012,248
Loss from operations	(535,973)	(569,208)	(648,919)
Interest income	36,506	26,688	11,074
Change in fair value of equity investments	(1,115)	397	(19,299)
Non-cash interest expense on liabilities for sales of future royalties	(63,041)	(66,004)	(43,015)
Other expense	(3,963)	(337)	(1,566)
Loss before income taxes	(567,586)	(608,464)	(701,725)
(Provision for) benefit from income taxes	(1,597)	1,825	(5,696)
Net loss	$ (569,183)	$ (606,639)	$ (707,421)

Net loss per share, basic and diluted	($ 6.29)	($ 8.25)	($ 10.12)
Shares used in computing net loss per share, basic and diluted	90,538,118	73,543,862	69,914,225

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Year Ended December 31,		
	2024	**2023**	**2022**
Net loss	($ 569,183)	($ 606,639)	($ 707,421)
Other comprehensive income (loss):			
Foreign currency translation adjustments	(1,044)	239	(724)
Changes in unrealized gain (loss) on available-for-sale securities	(246)	6,981	(4,445)
Other comprehensive income (loss):	(1,290)	7,220	(5,169)
Total comprehensive loss	($ 570,473)	($ 599,419)	($ 712,590)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(In thousands, except share amounts)	Common Stock		Additional Paid-In	Accumulated Other Comprehensive Income (Loss)	Accumulated	Treasury	Deferred Compensation	Total Stockholders'
	Shares	Amount	Capital		Deficit	Stock	Obligation	Equity
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
Issuance of common stock and pre-funded warrants in connection with underwritten public offering, net of issuance costs	9,833,334	10	326,446	—	—	—	—	326,456
Issuance of common stock in connection with at-the-market offering, net of issuance costs	1,175,584	1	53,298	—	—	—	—	53,299
Stock-based compensation	—	—	134,169	—	—	—	—	134,169
Issuance of common stock under equity plan awards, net of tax	1,109,375	1	8,414	—	—	—	—	8,415
Deferred compensation	—	—	—	—	—	(432)	432	—
Other comprehensive income	—	—	—	7,220	—	—	—	7,220
Net loss	—	—	—	—	(606,639)	—	—	(606,639)
Balance as of December 31, 2023	82,315,590	$ 82	$ 3,662,346	$ 647	$ (3,387,661)	$ (432)	$ 432	$ 275,414
Issuance of common stock and pre-funded warrants in connection with underwritten public offering, net of issuance costs	8,782,051	9	380,974	—	—	—	—	380,983

Stock-based compensation	—	—	158,115	—	—	—	—	158,115
Issuance of common stock under equity plan awards, net of tax	1,386,689	1	11,257	—	—	—	—	11,258
Deferred compensation	—	—	—	—	—	3,161	3,161	—
Other comprehensive loss	—	—	—	1,290	—	—	—	1,290
Net loss	—	—	—	—	569,183	—	—	569,183
Balance as of December 31, 2024	92,484,330	$ 92	$ 4,212,692	$ 643	$ 3,956,844	$ 3,593	$ 3,593	$ 255,297

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2024	**2023**	**2022**
Operating activities:			
Net loss	$ (569,183)	$ (606,639)	$ (707,421)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	158,030	135,227	130,377
Acquired in-process research and development	—	—	75,033
Amortization of premium (discount) on marketable debt securities, net	(12,624)	(12,842)	2,699
Depreciation and amortization	35,543	26,006	18,220
Change in fair value of equity investments	1,115	(397)	19,299
Non-cash collaboration royalty revenue	(100,539)	(69,364)	(21,692)
Non-cash interest expense on liabilities for sales of future royalties	63,041	66,004	43,015
Other	(3,489)	2,300	(230)
Changes in operating assets and liabilities:			
Accounts receivable	(33,598)	(22,778)	(12,068)
Inventory	(11,207)	(6,930)	(9,701)
Prepaid expenses and other assets	11,731	15,325	3,798
Accounts payable, accrued, and other liabilities	46,992	901	79,845
Deferred tax liabilities	—	(1,619)	(1,639)
Net cash used in operating activities	(414,188)	(474,806)	(380,465)
Investing activities:			
Purchase of property, plant, and equipment	(7,491)	(44,267)	(116,123)
Acquisition, net of cash acquired	—	—	(75,025)

Purchase of marketable debt securities	(408,613)	(526,382)	(614,735)
Proceeds from sale of marketable debt securities	3,247	50,672	84,275
Proceeds from sale of equity investments	—	—	10,094
Proceeds from maturities of marketable debt securities	410,025	695,525	450,706
Payment for intangible asset	(12,500)	(2,500)	(30,000)
Other	(2,436)	(5,048)	(844)
Net cash (used in) provided by investing activities	(17,768)	168,000	(291,652)
Financing activities:			
Proceeds from the sale of future royalties, net	—	—	490,950
Proceeds from the issuance of common stock and pre-funded warrants in connection with underwritten public offerings, net of issuance costs	380,983	326,456	—
Proceeds from the issuance of common stock in connection with at-the-market offering, net of issuances costs	—	53,299	—
Proceeds from the issuance of common stock from exercise of equity plan awards, net	11,258	8,415	10,813
Proceeds from issuance of equity interest in noncontrolling interest	7,000	—	—
Other	—	(28)	(555)
Net cash provided by financing activities	399,241	388,142	501,208
Effect of exchange rate changes on cash	(2,525)	462	(1,075)
Net (decrease) increase in cash, cash equivalents, and restricted cash	(35,240)	81,798	(171,984)
Cash, cash equivalents, and restricted cash at beginning of year	219,399	137,601	309,585
Cash, cash equivalents, and restricted cash at end of year	$ 184,159	$ 219,399	$ 137,601

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2024	**2023**	**2022**
Supplemental disclosures of non-cash investing and financing information:			
Acquired lease liabilities arising from obtaining right-of-use assets and property, plant, and equipment	$ 9,609	$ 22,162	$ 1,168
Costs of property, plant and equipment included in accounts payable, accrued, and other liabilities	$ 693	$ 1,577	$ 17,963
Non-cash interest expense on liabilities for sales of future royalties capitalized during the year into ending property, plant and equipment	$ —	$ 9,431	$ 11,380

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
Notes to Consolidated Financial Statements

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 ultrarare 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, and Japan for the treatment of homozygous familial hypercholesterolemia, or HoFH. The Company has exclusive rights 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;
- 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 Imperfecta, or OI;
- GTX-102 is an antisense oligonucleotide, or ASO 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; and
- 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.

The Company has sustained operating losses and expects such annual losses to continue in the near term. The Company's ultimate success depends on the outcome of its research and development and commercialization activities. Through December 31, 2024, 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 may need to raise additional capital to fully implement its business plans 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 the Company and its wholly-owned subsidiaries. The Company consolidates any variable interest entity, or VIE, for which it is the primary beneficiary.

Segment Reporting

The Company operates as one reportable segment relating to the research, development and commercialization of its products. The segment derives its current revenues from its four commercially approved products.

The Company's Chief Operating Decision Maker, or CODM, its Chief Executive Officer and the executive leadership team, manage the Company's operations on an integrated basis for the purposes of allocating resources. When evaluating the Company's financial performance, the CODM regularly reviews total revenues and total expenses and makes decisions using this information on a global basis.

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 to guarantee the fulfillment of certain sales orders to certain government-sponsored customers.

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 same such amounts shown in the Consolidated Statements of Cash Flows (in thousands):

	December 31,		
	2024	2023	2022
Cash and cash equivalents	$ 173,729	$ 213,584	$ 132,944
Restricted cash included in other current assets	6,806	2,008	862
Restricted cash included in other non-current assets	3,624	3,807	3,795
Total cash, cash equivalents, and restricted cash shown in the statements of cash flows	$ 184,159	$ 219,399	$ 137,601

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 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, using market quotes when 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 other assets 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.

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 financial instruments, the Company uses a forward-looking expected loss model that recognizes a current period charge for losses that are expected to be incurred over the life of the financial instrument.

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.

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. There was

no

allowance for losses on available-for-sale debt securities which were attributable to credit risk for the years ended December 31, 2024 and 2023.

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 when 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. 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. See "Note 4. Balance Sheet Components" for further disclosure on the useful lives of property, plant, and equipment.

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 annually and whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. 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.

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 material 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.

Liabilities for Sales of Future Royalties

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 11. Liabilities for Sales of Future Royalties." The Company recorded the liabilities at inception based upon estimated future cash flows discounted at a market rate. The liabilities are being amortized 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) to RPI and OMERS 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 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 employs the prospective method to adjust the amortization of the liabilities and the effective interest rate.

Revenue Recognition

Product Sales

The Company sells its approved products through a limited number of distributors. Under Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers,* revenue from product sales is recognized at the point in time when control is transferred 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.

Collaboration, License, and Royalty Revenue

The Company has certain license and collaboration agreements that are within the scope of 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.

The Company utilizes certain information from its collaboration partners to record collaboration revenue, 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.

As described in "Note 11. Liabilities for Sales of Future Royalties", for certain royalty payments from net sales of Crysvita in applicable territories that were sold to RPI and OMERS, the Company records the royalty revenue 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*, 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.

Deferred Compensation Plan

The Company maintains a nonqualified deferred compensation plan whereby certain employees and members of the board of directors are able to defer certain equity awards and other compensation. Amounts deferred are invested into shares of the Company's common stock and corporate-owned life insurance. The plan complies with the provisions of Section 409A of the Internal Revenue Code. All the investments held in the plan are recorded in other non-current assets in the Consolidated Balance Sheets. The short-term portion of the corresponding liability for the plan is included in accrued expenses. The long-term portion of the liability is included in other non-current liabilities in the Consolidated Balance Sheets. Changes in the value of the deferred compensation assets and liabilities are recorded in earnings as they occur. Certain equity awards deferred under the plan are required to be settled through the issuance of Company stock. These awards are recorded as treasury stock and deferred compensation obligation within stockholders' equity.

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 10. 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 is 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 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. Shares of common stock into which pre-funded warrants may be exercised are considered outstanding for the purposes of computing basic net loss per share because the shares may be issued for little or no consideration, are fully vested and are exercisable after the original issuance date. 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.

Recent Accounting Pronouncements

In November 2024, the FASB issued ASU 2024-03, *Income Statement-Reporting Comprehensive Income-Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses*, requiring public entities to disclose additional information about specific expense categories in the notes to the financial statements on an interim and annual basis. ASU 2024-03 is effective for fiscal years beginning after December 15, 2026, and for interim periods beginning after December 15, 2027, with early adoption permitted. The Company is currently evaluating the impact of adopting ASU 2024-03.

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, requiring public entities to disclose information about their reportable segments' significant expenses and other segment items on an interim and annual basis. Public entities with a single reportable segment are required to apply the disclosure requirements in ASU 2023-07, as well as all existing segment disclosures and reconciliation requirements in ASC 280 on an interim and annual basis. The Company adopted ASU 2023-07 during the year ended December 31, 2024.

3. Fair Value Measurements

Certain 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. The carrying amounts of liabilities for the sales of future royalties also approximate their fair value. 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 investment in 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, 2024			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 113,894	$ —	$ —	$ 113,894
Time deposits	—	10,000	—	10,000
Corporate bonds	—	391,731	—	391,731
Commercial paper	—	21,194	—	21,194
Asset-backed securities	—	143	—	143
U.S. Government Treasury and agency securities	—	158,814	—	158,814
Investment in Solid common stock	2,089	—	—	2,089
Deferred compensation assets	—	15,337	—	15,337
Total financial assets	$ 115,983	$ 597,219	$ —	$ 713,202
Financial Liabilities:				

Deferred compensation liabilities	$ —	15,756	$ —	15,756

	December 31, 2023			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 162,289	$ —	$ —	$ 162,289
Certificates of deposit and time deposits	—	17,986	—	17,986
Corporate bonds	—	215,166	—	215,166
Commercial paper	—	20,620	—	20,620
Asset-backed securities	—	2,712	—	2,712
U.S. Government Treasury and agency securities	57,437	259,605	—	317,042
Investment in Solid common stock	3,204	—	—	3,204
Deferred compensation assets	—	10,220	—	10,220
Total financial assets	$ 222,930	$ 526,309	$ —	$ 749,239
Financial Liabilities:				
Deferred compensation liabilities	$ —	$ 10,365	$ —	$ 10,365

Deferred compensation liabilities consist of short-term liabilities of $ 0.6 million and $ 0.2 million as of December 31, 2024 and 2023, respectively, included in accrued liabilities on the Consolidated Balance Sheets, and long-term liabilities of $ 15.2 million and $ 10.1 million as of December 31, 2024 and 2023, respectively, included in other non-current liabilities on the Consolidated Balance Sheets. There have been no significant net gains or losses on deferred compensation assets or liabilities for the periods presented.

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, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value

Money market funds	$ 113,894	$ —	$ —	$ 113,894
Time deposits	10,000	—	—	10,000
Corporate bonds	391,124	809	(202)	391,731
Commercial paper	21,194	—	—	21,194
Asset-backed securities	143	—	—	143
U.S. Government Treasury and agency securities	158,414	404	(4)	158,814
Total	$ 694,769	$ 1,213	$ (206)	$ 695,776

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Losses	Estimated Fair Value
Money market funds	$ 162,289	$ —	$ —	$ 162,289
Certificates of deposit and time deposits	17,986	—	—	17,986
Corporate bonds	214,792	711	(337)	215,166
Commercial paper	20,620	—	—	20,620
Asset-backed securities	2,715	—	(3)	2,712
U.S. Government Treasury and agency securities	316,160	982	(100)	317,042
Total	$ 734,562	$ 1,693	$ (440)	$ 735,815

At December 31, 2024, 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. All marketable securities with unrealized losses at December 31, 2024 have been in a loss position for less than 12 months or the loss is not material and is temporary in nature.

Inventory

Inventory consists of the following (in thousands):

	December 31, 2024	2023
Work-in-process	$ 21,967	$ 18,859
Finished goods	23,040	15,110
Total inventory	$ 45,007	$ 33,969

Property, Plant, and Equipment, net

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

	Useful life (years)	December 31, 2024	2023
Building	20 - 30	$ 181,576	$ 181,356
Leasehold improvements	Shorter of lease term or estimated useful life	58,021	58,683
Research and development equipment	5	60,233	56,347
Furniture and office equipment	5	6,475	6,419
Computer equipment and software	3 - 5	16,365	16,196
Manufacturing equipment	5 - 15	37,332	37,297

Land	Not applicable	16,619	16,619
Other	Varies by asset	1,790	1,050
Property, plant, and equipment, gross		378,411	373,967
Less: accumulated depreciation		(112,482)	(83,401)
Property, plant, and equipment, net		$ 265,929	$ 290,566

Depreciation expense for the years ended December 31, 2024, 2023, and 2022 was $ 30.1 million, $ 22.2 million and $ 15.0 million, respectively. Amortization of leasehold improvements and software is included in depreciation expense.

Accrued Liabilities

Accrued liabilities consists of the following (in thousands):

	December 31, 2024	2023
Research, clinical study, and manufacturing expenses	$ 88,133	$ 65,326
Payroll and related expenses	94,021	82,936
Revenue related reserves	33,344	17,029
Other	25,475	31,195
Total accrued liabilities	$ 240,973	$ 196,486

5. Intangible Assets, net

Indefinite-lived Intangibles

As a result of the accounting for our acquisition of Dimension Therapeutics, Inc. in November 2017, the Company has IPR&D assets of $ 129.0 million as of December 31, 2024 and 2023. 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. 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 total useful life of 6 years.

In January 2022, the Company announced a collaboration with Regeneron to commercialize Evkeeza for HoFH outside of the U.S. Pursuant to the collaboration agreement, the Company has incurred an upfront payment and regulatory and sales milestones to date totaling $ 57.5 million. As these payments are for the Company's use of intellectual property for Evkeeza for HoFH, they were recorded as intangible assets, which are amortized over a weighted-average total useful life of 9 years.

The Company's intangible assets were as follows:

	December 31, 2024			
	Gross Carrying Amount	Weighted-Average Life (Years)	Accumulated Amortization	Net Carrying Amount
Indefinite-lived intangibles	$ 129,000	—	$ —	$ 129,000
Finite-lived intangibles	62,275	9	(12,961)	49,314
Total intangible assets	$ 191,275	—	$ (12,961)	$ 178,314

	December 31, 2023			
	Gross Carrying Amount	Weighted-Average Life (Years)	Accumulated Amortization	Net Carrying Amount
Indefinite-lived intangibles	$ 129,000	—	$ —	$ 129,000
Finite-lived intangibles	44,775	10	(7,504)	37,271
Total intangible assets	$ 173,775	—	$ (7,504)	$ 166,271

The Company recorded costs of sales of $ 5.5 million, $ 3.8 million and $ 3.2 million for the years ended December 31, 2024, 2023, and 2022, respectively, related to the amortization of the intangible assets.

The expected amortization of the intangible assets, as of December 31, 2024, for each of the next five years and thereafter is as follows:

2025	$ 7,162
2026	7,162
2027	6,722

2028	6,282
2029	6,282
Thereafter	15,704
Total	$ 49,314

6. Revenue

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

	Year Ended December 31,		
	2024	2023	2022
Product sales:			
Crysvita	$ 134,709	$ 75,697	$ 42,678
Dojolvi	88,194	70,633	55,612
Evkeeza	32,162	3,642	—
Mepsevii	30,350	30,441	20,637
Total product sales	285,415	180,413	118,927
Crysvita royalty revenue	274,815	182,652	21,692
Collaboration and license revenue:			
Crysvita collaboration revenue in Profit-Share Territory	—	69,705	215,024
Other	—	1,479	7,686
Total collaboration and license revenue	—	71,184	222,710
Total revenues	$ 560,230	$ 434,249	$ 363,329

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

	Year Ended December 31,		
	2024	2023	2022
North America	$ 340,463	$ 307,149	$ 281,088
Latin America	130,713	77,342	44,711
Europe, Middle East, and Africa	80,124	47,534	36,369

Asia-Pacific	8,930	2,224	1,161
Total revenues	$ 560,230	$ 434,249	$ 363,329

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

	Year Ended December 31,		
	2024	2023	2022
Balance of product sales reserve at beginning of year	$ 17,029	$ 11,487	$ 7,181
Provisions	38,102	18,761	13,525
Payments	(21,391)	(12,746)	(9,613)
Adjustments	(434)	(473)	394
Balance of product sales reserve at end of year	$ 33,306	$ 17,029	$ 11,487

The following table presents changes in the contract liabilities for the years ended December 31, 2023 (in thousands):

	December 31, 2023
Balance of contract liabilities at beginning of period	$ 1,479
Additions	—
Deductions	(1,479)
Balance of contract liabilities at end of period, net	$ —

See “Note 9. License and Research Agreements” for additional details on contract liabilities activities.

The Company’s largest accounts receivable balance was from a collaboration partner, KKC, and was

70
% and

53
% of the total accounts receivable balance as of December 31, 2024 and 2023, respectively.

7. Investment in Amlogenyx. Inc.

In July 2024, the Company contributed certain intellectual property rights to Amlogenyx Inc., or Amlogenyx, a subsidiary of the Company, and received

9.0
million shares of common stock of Amlogenyx. A third-party investor along with one of its affiliated entities, and the Company, each contributed $

7.0
million to Amlogenyx and in exchange, each received approximately

1.6
million

shares of series seed preferred stock of Amlogenyx. The purpose of Amlogenyx is to pursue the application of the Company's novel adeno-associated virus, or AAV, gene therapy to treat beta-amyloid disorders and related neurodegenerative diseases.

Amlogenyx was determined to be a VIE and the Company is the primary beneficiary as it has the power to direct the activities that would most significantly impact the economic performance of Amlogenyx, including the performance of R&D activities relating to its sole product candidate. As the primary beneficiary, the Company has consolidated the financial position, results of operations and cash flows of Amlogenyx in its financial statements and all intercompany balances have been eliminated in consolidation. Upon initial consolidation, the non-controlling interest of the third-party investor was recorded at its estimated fair value of $

7.0
million, which is equal to their original investment.

As of December 31, 2024, total assets and liabilities included on the Consolidated Balance Sheets for Amlogenyx were $

13.5
million and $

0.1
million, respectively. The assets primarily consisted of cash and cash equivalents which may only be used to settle obligations of Amlogenyx.

Noncontrolling interest related to the third-party investment in Amlogenyx is reported on the Consolidated Balance Sheets in mezzanine equity.

Changes in the carrying value of noncontrolling interest for the year ended December 31, 2024, were as follows:

	Noncontrolling Interest
As of December 31, 2023	$ —
Issuance of equity from noncontrolling interest	7,000
As of December 31, 2024	$ 7,000

In October 2024, Amlogenyx granted

778,500
stock options to its employees from its 2024 Equity Incentive Plan, which authorizes

1,358,060
shares for issuance. For the year ended December 31, 2024, stock-based compensation related to these awards was immaterial.

8. 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. In July 2022, pursuant to the terms of the Unitholder Option Agreement, as amended, the Company exercised the 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. During the year ended December 31, 2024, the Company achieved a $

30.0
million regulatory milestone upon the initiation of the Phase 3 *Aspire* clinical study for GTX-102. The Company is obligated to pay 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, contingent upon the achievement of the milestones. 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 unitholders are 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.

As part of the Company's acquisition of GeneTx, the Company assumed a License Agreement with Texas A&M University, or TAMU. To date, the Company recognized an aggregate of $

0.5
million for clinical milestones under the TAMU agreement, and have in aggregate up to $

23.0

million of future obligations for various future milestones and a nominal annual license fee that may increase up to a maximum of $

2.0

million. The Company will also pay mid-single-digit percentage royalties based on licensed product annual net sales. As of December 31, 2024 and 2023, the Company had $

0.5

million and

nil

, respectively, in collaboration payables under this arrangement.

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, to date, amounts paid to acquire GeneTx, net of cash and working capital acquired, were classified as in-process research and development expense.

9. 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. 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, UK, 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.

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

Product Sales Revenue for Latin America and Turkey

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 for the sale of Crysvita once the product is delivered and the risk and title of the product is transferred to the distributor. In Turkey, KKC has the option to assume responsibility for commercialization efforts.

Transfer Price and Royalties on Product Sales Revenue

Under the collaboration agreement, KKC manufactures and supplies Crysvita, which is purchased by the Company for sales in Latin America and Turkey, and charges the Company a transfer price of

30
% of net sales. The transfer price on these sales was

35
% prior to December 31, 2022. The Company also pays to KKC a low single-digit royalty on net sales in Latin America.

Collaboration and Royalty Revenue for Sales in the Profit-Share Territory

The Company and KKC shared commercial responsibilities and profits in the Profit-Share Territory until April 2023. Under the collaboration agreement, KKC manufactured and supplied Crysvita for commercial use in the Profit-Share Territory and charged the Company a transfer price of

30
% of net sales in 2023, and

35
% prior to December 31, 2022. The remaining profit or loss after supply costs from commercializing products in the Profit-Share Territory was 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 transitioned to KKC. Thereafter, the Company is entitled to receive a tiered double-digit revenue share from the mid-

20
% range up to a maximum rate of

30
%.

The parties subsequently agreed that the Company would have the right to continue to support KKC in commercial field activities in the U.S. through January 31, 2025, as amended. After January 31, 2025, the Company's rights to promote Crysvita in the U.S. are limited to medical geneticists and the Company solely bears its expenses for the promotion of Crysvita in the Profit-Share Territory.

During the prior profit-share period, as KKC was the principal in the sale transaction with the customer, the Company recognized a pro-rata share of collaboration revenue, net of transfer pricing, in the period the sale occurred. The Company concluded that its portion of KKC's sales in the Profit-Share Territory prior to April 2023 was analogous to a royalty and therefore recorded its share as collaboration revenue, similar to a royalty. Starting in April 2023, the Company began to record as royalty revenue in the period the underlying sales occurred.

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 11. Liabilities for Sales of Future Royalties."

Royalty Revenue for 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 11. 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. The Company records this revenue as royalty revenue.

Total Crysvita revenue was as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Product sales	$ 134,709	$ 75,697	$ 42,678
Revenue in profit-share territory:			
Royalty revenue	174,276	113,288	—
Non-cash royalty revenue	74,690	48,581	—
Collaboration revenue	—	69,705	215,024
Total revenue in Profit-Share Territory	248,966	231,574	215,024
Non-cash royalty revenue in European Territory	25,849	20,783	21,692
Total Crysvita revenue	$ 409,524	$ 328,054	$ 279,394

Development Activities

In the field of orphan diseases, except for ongoing studies being conducted by KKC, the Company was the lead party for development activities in the Profit-Share Territory and in the European Territory until the applicable transition date. The Company shared 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 was the transition date for the Profit-Share Territory, KKC became the lead party and became responsible for the costs of the subsequent development activities. However, the Company will continue to equally share in the costs of the studies with KKC that commenced prior to the applicable transition date.

Collaboration Cost Sharing and Payments

Under the collaboration agreement, KKC and the Company share certain development and commercialization costs, and as a result, the Company was reimbursed for these costs and operating expenses were reduced. KKC also receives a transfer price and royalty on net product sales revenue which is recorded in cost of sales. These amounts were recognized in the Company's Statements of Operations in connection with the collaboration agreement with KKC as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Research and development	$ (3,670)	$ (6,510)	$ (15,974)
Selling, general and administrative	$ (4,082)	$ (17,199)	$ (37,217)
Cost of sales	$ 46,027	$ 18,476	$ 13,250

Collaboration Receivable and Payable

The Company had accounts receivable from KKC in the amount of $

85.4
million and $

39.2
million from profit-share revenue and royalties and other receivables recorded in other current assets of $

1.8
million and $

1.1
million and accrued liabilities of $

7.1
million and $

5.3
million from amounts owed for transfer price and royalties as well as commercial and development activity reimbursements, as of December 31, 2024 and 2023, respectively.

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 for the treatment of LC-FAOD.

During the year ended December 31, 2022, the Company recorded $

2.5
million for the attainment of a commercial milestone as a finite-lived intangible asset. 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 pays BRI a mid- single-digit royalty on net sales of the licensed product in the licensed territories.

Regeneron

In January 2022, the Company announced a collaboration with Regeneron to commercialize Evkeeza for HoFH outside of the U.S. 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 paid Regeneron a $

30.0
million upfront payment. As of December 31, 2024 the Company has recognized an aggregate of $

27.5
million for regulatory and sales milestones under the agreement, of which $

15.0

million was achieved during the year ended December 31, 2024. As these payments are for the Company's use of intellectual property for Evkeeza for HoFH, they were recorded as intangible assets. See "Note 5. Intangible Assets, net" for additional details. Going forward, the Company is obligated to pay Regeneron up to an aggregate of $

35.5

million of future obligations for additional regulatory and sales milestones, if achieved. The Company may share in certain costs for global trials led by Regeneron and also received the right to opt into other potential indications. Additionally, the Company pays Regeneron a transfer price fee and royalties on certain revenues.

The collaboration agreement is within the scope of ASC 808 which provides guidance on the presentation and disclosure of collaborative arrangements. As the Company is the principal in sales transactions with the customer, the Company recognizes 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 supplies the product and charges the Company a transfer price from the low

20

% range up to

40

% on net sales, which is recognized as cost of sales in the Company's Statement of Operations.

Under the collaboration agreement, Regeneron and the Company share certain development and commercialization costs. Regeneron also receives a transfer price and royalty on net product sales revenue which is recorded in cost of sales. These amounts were recognized in the Company's Statements of Operations in connection with the collaboration agreement with Regeneron as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Research and development	$ (2,842)	$ 7,629	$ 7,258
Cost of sales	$ 8,030	$ 684	$ —

The Company had collaboration payables for this arrangement included in accrued liabilities on the Consolidated Balance Sheets of $

17.8

million and $

10.6

million as of December 31, 2024 and December 31, 2023, 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.

Under the license agreement, the Company is obligated to pay to SLU a low single-digit royalty on net sales of the licensed products in Europe and Japan, subject to certain potential deductions. The Company's obligation to pay royalties to SLU in these territories continues until the expiration of any orphan drug exclusivity.

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, the Company is obligated to pay tiered royalties of up to

10

% on net sales and commercial milestone payments of up to $

30.0

million contingent upon 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, the Company is obligated to pay up to $

1.0

million contingent upon achievement of development and regulatory milestones as well as royalties in the low single-digits of net sales.

The Company paid Abeona $

3.1

million for prior development and transition costs which were recorded as research and development expense for the year ended December 31, 2022.

Mereo

In December 2020, the Company entered into a License and Collaboration Agreement with Mereo to collaborate on the development of setrusumab. Under the terms of the agreement, as amended, 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, or the Ultragenyx Territory, excluding the EEA, UK, and Switzerland, or the Mereo Territory, where Mereo retains commercial rights. Each party will be responsible for post-marketing

commitments in their respective territories and Ultragenyx will be responsible for commercial supply in both the Ultragenyx Territory and Mereo Territory.

Upon the closing of the transactions under the License and Collaboration Agreement with Mereo in January 2021, the Company made a payment of $

50.0
million to Mereo. To date, the Company has made payments totaling $

9.0
million for regulatory milestones achieved. The Company is obligated to pay Mereo up to $

245.0
million in future milestone payments, contingent upon the achievement of certain regulatory and commercial milestones. The Company pays for all global development costs and will pay a tiered double-digit percentage royalties to Mereo on net sales in the Ultragenyx Territory. Mereo will pay the Company a fixed double-digit percentage royalty on net sales in the Mereo Territory. If the Company receives and resells an FDA PRV in connection with a new drug application approval, Mereo is entitled to receive a portion of proceeds from the sale of the PRV or a cash payment from the Company, in the event the Company chooses to retain the PRV.

In December 2024, the Company entered into a manufacturing and supply agreement with Mereo where it is responsible for the supply of setrusumab to Mereo in the Mereo territory. Mereo is responsible to reimburse us for a portion of the manufacturing process development costs as well as future commercial supply costs.

Although Mereo is a VIE, 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.

For the year ended December 31, 2024, the Company recorded an offset to research and development expense of $

0.9
million. For the year ended December 31, 2023, the Company recorded development costs of $

9.0
million for the achievement of a clinical milestone recorded in research and development expense.

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 is obligated to make milestone payments of up to $

5.0
million for each indication, if certain development milestones are achieved. 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.

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 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, which are 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 a nominal annual maintenance fee 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. The Company is obligated to pay nominal annual fees, milestone payments of up to $

14.0
million contingent upon achievement, 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.

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 holds

521,719
shares of Solid's common stock. 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 VIE, 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, 2022	$ 2,807
Change in fair value	397
December 31, 2023	3,204
Change in fair value	(1,115)
December 31, 2024	$ 2,089

Arcturus Therapeutics Holdings Inc.

The Company previously held an investment in shares of common stock from Arcturus Therapeutics Holdings Inc., or Arcturus, which was accounted at fair value, as the fair value was readily determinable. During the year ended December 31, 2022, the Company sold

500,000
shares of Arcturus common stock, at a weighted-average price of $

20.39
per share. As of December 31, 2024 and 2023, the Company held

no
shares of Arcturus common stock.

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

	Arcturus Common Stock

December 31, 2021	$	18,505
Change in fair value		(8,411)
Sale of shares		(10,094)
December 31, 2022	$	—

10.Leases

The Company leases office space and research, testing and manufacturing laboratory space in various facilities in Novato and Brisbane, California, in Somerville and Woburn, Massachusetts, and in certain foreign countries, under operating agreements expiring at various dates through 2029 . Certain lease agreements include options for the Company to extend the lease for multiple renewal periods and 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,		
	2024	**2023**	**2022**
Operating lease expense	$ 11,985	$ 12,883	$ 11,775
Variable lease expense	5,893	5,272	4,785
Financing:			
Amortization	—	203	343
Interest expense	—	—	37
Total	$ 17,878	$ 18,358	$ 16,940

Cash paid for amounts included in the measurement of operating lease liabilities for the years ended December 31, 2024, 2023, and 2022 was $

16.1
million, $

13.4
million, and $

13.1
million, respectively, and was included in net cash used in operating activities in the Consolidated Statements of Cash Flows.

Right-of-use lease assets were $

25.5
million and $

23.9
million as of December 31, 2024 and 2023, respectively, and were included in other non-current assets on the Consolidated Balance Sheets.

The following table summarizes maturities of lease liabilities and the reconciliation of lease liabilities as of December 31, 2024:

Year Ending December 31,	**Operating**
2025	$ 13,831
2026	13,949
2027	9,019
2028	6,709
2029	5,589
Thereafter	467
Total future lease payments	49,564
Less: Amount representing interest	(9,225)

Present value of future lease payments	40,339
Less: Lease liabilities, current	(10,297)
Lease liabilities, non-current	$ 30,042

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, 2024 and 2023, the weighted-average remaining operating lease terms were 4 years and 5 years, respectively, the weighted-average discount rates used to determine the lease liability for operating leases were

10.1
% and

9.6
%, respectively.

11. 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 is 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. The Company records the royalty revenue arising from the net sales of Crysvita in the applicable territories as royalty revenue in the Consolidated Statements of Operations over the term of the arrangements. Royalties earned under the RPI and OMERS arrangements from inception to December 31, 2024

have been $

99.3
million and $

123.3
million, respectively. The Company's effective annual interest rates were

6.2
% and

7.5
%, for RPI and OMERS, respectively, as of December 31, 2024.

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, 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 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 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, 2022	$ 365,189	$ 510,250	$ 875,439
Royalty revenue	(20,783)	(38,524)	(59,307)
Non-cash interest expense	32,235	43,200	75,435
December 31, 2023	376,641	514,926	891,567
Royalty revenue	(25,849)	(59,088)	(84,937)
Non-cash interest expense	23,747	39,294	63,041
December 31, 2024	$ 374,539	$ 495,132	$ 869,671

12.Equity

At-the-Market Offerings

In February 2024, the Company entered into a Sales Agreement with Cowen and Company, LLC, or Cowen, 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 at-the-market, or ATM, offerings through Cowen.

No
shares were sold under this agreement during the year ended December 31, 2024.

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. During the year ended December 31, 2023, there were

1,175,584
shares sold under the ATM resulting in net proceeds of $

53.3
million.

Underwritten Public Offering

In June 2024, the Company completed an underwritten public offering in which

8,782,051
shares of common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional

1,346,153
shares, at a public offering price of $

39.00
per share. In connection with the offering, the Company sold to certain investors pre-funded warrants, in lieu of common stock, to purchase

1,538,501
shares of common stock at a purchase price of $

38.999
per pre-funded warrant, which equals the public offering price per share of common stock less the $

0.001
exercise price per share of each pre-funded warrant. The total proceeds that the Company received from the offering were $

381.0
million, net of underwriting discounts and commissions.

The pre-funded warrants were classified as a component of permanent equity in the Company's Consolidated Balance Sheets as they are freestanding financial instruments that are immediately exercisable, do not embody an obligation for the Company to repurchase its own shares and permit the holders to receive a fixed number of shares of common stock upon exercise. All of the shares underlying the pre-funded warrants have been included in the weighted-average number of shares of common stock used to calculate net loss per share, basic and diluted, attributable to common stockholders because the shares may be issued for little or no

consideration, are fully vested, and are exercisable after the original issuance date of the pre-funded warrants. As of December 31, 2024,

no
ne of the pre-funded warrants had been exercised.

The table below summarizes pre-funded warrants activity:

	Pre-funded warrants
As of December 31, 2022	—
Issuance of pre-funded warrants	1,666,722
As of December 31, 2023	1,666,722
Issuance of pre-funded warrants	1,538,501
As of December 31, 2024	3,205,223

In October 2023, the Company completed an underwritten public offering in which

9,833,334
shares of common stock were sold, including the exercise in full by the underwriters of their option to purchase an additional

1,500,000
shares, at a public offering price of $

30.00
per share. In connection with the offering, the Company sold to certain investors pre-funded warrants, in lieu of common stock, to purchase

1,666,722
shares of common stock at a purchase price of $

29.999
per pre-funded warrant, which equals the public offering price per share of common stock less the $

0.001
exercise price per share of each pre-funded warrant. The total proceeds that the Company received from the offering were $

326.5
million, net of underwriting discounts and commissions.

13. Stock-Based Awards

Equity Plan Awards

Under the terms of the Company's 2023 Incentive Plan, or 2023 Plan, and Employment Inducement Plan, or Inducement Plan, awards may be granted at an exercise price not less than fair market value. The exercise price of an option may not be less than the fair market value. The term of an award granted under the 2023 Plan and Inducement Plan may not exceed ten years . Typically, the vesting schedule for option grants to 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 .

Under the 2014 Employee Stock Purchase Plan, or ESPP, 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, 2024, the Company issued

200,539
shares of common stock under the ESPP.

The table below summarizes the Company's equity plans as of December 31, 2024:

Plan	Year of Adoption	Expiration Date, as Amended	Maximum Number of Shares Authorized	Shares Available for Future Issuance
Employment Inducement Plan	2021	February 3, 2031	1,200,000	211,628

2023 Incentive Plan[1]	2023	June 7, 2023	10,475,837	6,139,766
2014 Employee Stock Purchase Plan	2014	June 7, 2033	7,330,914	6,409,256

(1) Maximum number of shares authorized and shares available for future issuance under the 2023 Incentive Plan include

1,975,837
shares subject to the 2014 Incentive Plan cancelled after

June 7, 2023
.

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, 2023	8,787,712	$ 67.43	6	$ 7,558
Options granted	1,445,364	52.91		
Options exercised	(124,536)	46.06		
Options cancelled	(747,571)	66.68		
Outstanding — December 31, 2024	9,360,969	65.54	6	1839
Vested and exercisable — December 31, 2024	6,360,538	71.27	5	729
Vested and expected to vest — December 31, 2024	9,096,200	65.95	6	1,742

The following table summarizes the Company's options exercised and vested for each of the periods indicated (in thousands except for weighted-average estimated fair value of options granted):

	Year Ended December 31,		
	2024	2023	2022
Intrinsic value of options exercised	$ 862	$ 4,950	$ 2,552
Cash received from the exercise of options	$ 5,736	$ 2,743	$ 6,242
Weighted-average estimated fair value of options granted	$ 29.88	$ 25.53	$ 34.77
Estimated fair value of options vested	$ 53,838	$ 59,663	$ 58,677

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.

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, 2023	1,380,998	$ 67.37	3	$ —
PSOs cancelled	(135,707)	67.37		
Outstanding — December 31, 2024	1,245,291	67.37	2	—
Vested and exercisable — December 31, 2024	422,594	67.37	2	—
Vested and expected to vest — December 31, 2024	930,420	67.37	2	—

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, 2024, 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. The total estimated grant date fair value of PSOs vested during the years ended December 31, 2024 and 2023, was $

9.9
million and $

3.4
million, respectively. No PSOs were granted or exercised during the years ended December 31, 2024 and 2023. 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, 2023	3,444,112	$ 55.21
RSUs granted	3,169,688	53.06
RSUs vested	(1,043,199)	59.92
RSUs cancelled	(400,654)	54.13
Unvested — December 31, 2024	5,169,947	53.22

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, 2024, 2023, and 2022 was $

62.5
million, $

54.6
million, and $

47.1
million, respectively. The aggregate intrinsic value of the shares of the RSUs vested during the years ended December 31, 2024, 2023, and 2022 was $

54.0
million, $

33.0
million, and $

37.8
million, respectively.

Performance Stock Units

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

	PSUs Outstanding	
	Number of Shares	**Weighted-Average Grant Date Fair Value**

Unvested — December 31, 2023	506,106	$ 60.82
PSUs granted	274,484	62.60
PSUs vested	(47,464)	72.17
PSUs cancelled	(114,944)	68.07
Unvested — December 31, 2024	618,182	59.39

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. 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, 2024, certain 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, 2024, 2023, and 2022 was $

3.4
million, $

3.9
million, and $

1.6
million, respectively, with an aggregate intrinsic value of the shares of $

2.1
million, $

1.3
million and $

2.0
million, respectively.

Stock-Based Compensation Expense

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

	Year Ended December 31,		
	2024	2023	2022
Cost of sales	$ 1,469	$ 1,166	$ 902
Research and development	86,616	74,531	74,464
Selling, general and administrative	69,971	59,516	55,002
Total stock-based compensation expense	$ 158,056	$ 135,213	$ 130,368

Stock-based compensation of $

2.6
million, $

1.9
million, and $

2.2
million was capitalized into inventory for the years ended December 31, 2024, 2023, and 2022, respectively. Capitalized stock-based compensation is recognized as cost of sales when the related product is sold.

As of December 31, 2024, the total unrecognized compensation expense related to unvested equity awards, net of estimated forfeitures, was $

256.8
million, which the Company expects to recognize over an estimated weighted-average period of 2 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,		
	2024	2023	2022
Expected term (years)	6	6	6
Expected volatility	55 %	55 %	56 %
Risk-free interest rate	4.2 %	4.2 %	2.0 %
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 in years	4
Expected volatility	57 %
Risk-free interest rate	1.5 %
Expected dividend rate	0.0 %

14. 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 $

9.8
million, $

9.7
million, and $

9.0
million as expense related to the plan for the years ended December 31, 2024, 2023, and 2022, respectively.

15. Income Taxes

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

	Year Ended December 31,		
	2024	2023	2022
Domestic	$ 564,072	$ 608,166	$ 703,411
Foreign	3,514	298	(1,686)
Total loss before income taxes	$ 567,586	$ 608,464	$ 701,725

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

	Year Ended December 31,		
	2024	2023	2022
Current provision for income taxes:			
Federal	$ —	$ —	$ —
State	224	(3,187)	6,062
International	2,745	3,127	1,274
Total current tax provision	2,969	(60)	7,336
Deferred tax provision:			
Federal	—	—	—
State	—	(1,608)	(1,640)
International	(1,372)	(157)	—
Total deferred tax provision	(1,372)	(1,765)	(1,640)
Total provision for (benefit from) income taxes	$ 1,597	$ (1,825)	$ 5,696

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 15 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. For the year ended December 31, 2023, the Company recognized an income tax benefit of $

4.8

million attributable to modifications in its state apportionment methodology, and then offset by an income tax expense of $

3.0
million from foreign jurisdictions. For the year ended December 31, 2024, the Company recognized an income tax expense of $

0.2
million for state tax, and income tax expense of $

1.4
million from foreign jurisdictions.

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

	Year Ended December 31,		
	2024	2023	2022
	%	%	%
Federal statutory income tax rate	21.0	21.0	21.0
State income taxes, net of federal benefit	—	0.8	(0.4)
Federal tax credits	10.8	7.3	5.9
Other	0.1	(0.7)	(0.1)
Nondeductible permanent items	(1.1)	(0.3)	(0.6)
Stock-based compensation	(1.6)	(1.8)	(1.2)
Uncertain tax positions	(2.0)	(1.4)	(1.2)
Change in valuation allowance	(27.1)	(24.1)	(24.0)
Foreign rate differential	(0.4)	(0.5)	(0.2)
Provision for income taxes	(0.3)	0.3	(0.8)
	%	%	%

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, 2024	2023
Deferred tax assets:		
Loss carryforwards	$ 309,301	$ 266,253
Tax credits	369,988	305,198
Stock options	51,939	44,795
Accruals and reserves	32,140	27,694
Fixed assets and intangibles	32,391	33,853
Liabilities for sales of future royalties	196,664	205,400
Basis difference in equity investments	8,683	8,423
Capitalized research and development costs	211,969	149,898
Other	589	281
Gross deferred tax assets	1,213,664	1,041,795
Valuation allowance	(1,206,514)	(1,035,836)
Total deferred tax assets	7,150	5,959
Deferred tax liabilities:		
In-process research and development	(30,058)	(30,688)
Right-of-use lease assets	(5,778)	(5,329)

Gross deferred tax liabilities	(35,836)	(36,017)
Net deferred tax liabilities	$ (28,686)	$ (30,058)

As of December 31, 2024 and 2023, the Company had approximately $

1,190.5
million and $

1,004.8
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, 2024 and 2023, the Company had approximately $

744.4
million and $

659.9
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, 2024 and 2023, the Company had federal research tax credit carryforwards of approximately $

45.1
million and $

46.9
million, respectively, available to reduce future tax liabilities that will begin to expire in 2031 . As of December 31, 2024 and 2023, the Company had state research credit carryforwards of $

92.0
million and $

74.4
million, respectively, available to reduce future tax liabilities that will be carried forward indefinitely.

As of December 31, 2024 and 2023, the Company had federal Orphan Drug Credits of $

338.5
million and $

269.6
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 $

170.7
million and $

141.3
million during the years ended December 31, 2024 and 2023, 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,		
	2024	2023	2022
Balance at beginning of year	$ 79,998	$ 66,794	$ 55,360
Additions based on tax positions related to current year	14,825	12,562	11,316

Additions for tax positions of prior years	2,173	642	377
Reductions for tax positions of prior years	—	—	(259)
Balance at end of year	$ 96,996	$ 79,998	$ 66,794

Approximately $

1.3
million in unrecognized tax benefits would impact the Company's effective tax rate if recognized. The Company has elected to include interest and penalties as a component of tax expense. For the years ended December 31, 2024 and 2023, the Company recognized accrued interest and penalties of $

0.1
million and $

0.2
million, respectively, as a component of income tax expense.

No
accrued interest and penalties were recognized as a component of income tax expense during the year ended December 31, 2022. 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, 2024, the Company had not made a provision for any incremental foreign withholding taxes on approximately $

13.0
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, 40 state tax jurisdictions, and ten foreign countries. The federal and state income tax returns from inception to December 31, 2024 remain subject to examination.

16. 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, 2024, the aggregate payments under contractually-binding manufacturing and service agreements are as follows (in thousands):

	Year Ended December 31,		
	2025	**2026**	**Total**
Manufacturing and Services	$ 33,842	$ 9,145	$ 42,987

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 9. License and Research Agreements."

See "Note 10. Leases" for lease commitments.

Contingencies

In the ordinary course of business, the Company may become party to various claims and complaints. See "Item 3. Legal Proceedings" for material legal proceedings the Company is aware of. The process of resolving matters through litigation or other means is inherently uncertain, however management does not believe that any ultimate liability resulting from any of these potential claims will have a material adverse effect on its results of operations, financial position, or liquidity.

Guarantees and Indemnifications

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

17. Related Party Transaction

In July 2022, the Company entered into an agreement with a non-profit foundation in which two members of the Company's board of directors, including the Company's Chief Executive Officer, at the time also served as board members of the foundation, whereby an aggregate $

1.0
million contribution is being paid 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, $

0.3
million, and $

0.3
million as research and development expense for this agreement for the years ended December 31, 2024, 2023, and 2022, respectively.

18. 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, 2024, 2023, and 2022 (in thousands, except share and per share data):

	Year Ended December 31,		
	2024	**2023**	**2022**
Numerator:			
Net loss	$ (569,183)	$ (606,639)	$ (707,421)
Denominator:			
Weighted-average shares used to compute net loss per share, basic and diluted	90,538,118	73,543,862	69,914,225
Net loss per share, basic and diluted	$ (6.29)	$ (8.25)	$ (10.12)

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

	Year Ended December 31,		
	2024	**2023**	**2022**
Options to purchase common stock, restricted stock units, and performance stock units	16,284,470	14,152,286	11,290,935
Employee stock purchase plan	7,790	8,450	7,581
	16,292,260	14,160,736	11,298,516

19. Accumulated Other Comprehensive (Loss) Income

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

	Year Ended December 31,	
	2024	**2023**
Cumulative foreign currency translation adjustment	$ (1,650)	$ (606)

Unrealized gain (loss) on securities available-for-sale	1,007	1,253
Total accumulated other comprehensive (loss) income	$ (643)	$ 647

Exhibit 10.15

[***] = 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.

November 18, 2020

KYOWA KIRIN INC. (1)

AND

ULTRAGENYX PHARMACEUTICAL INC. (2)

SUPPLY AGREEMENT

CONTENTS

Clause Heading Page

THIS AGREEMENT is made on October 27, 2020

BETWEEN

(1) Kyowa Kirin, Inc., a corporation organized and existing under the laws of Delaware, having its principal office at 135 Route 202/206, Suite 6 Bedminster, New Jersey 07921,
USA ("**Kyowa Kirin**"); and

(2) ULTRAGENYX PHARMACEUTICAL INC. a company organised and existing under the laws of Delaware, USA with an address at 60 Leveroni Ct, Novato, CA, 94949, USA and its affiliates (collectively referred to herein as "**UGNX**")

BACKGROUND

(A) Kyowa Kirin's parent company Kyowa Kirin Co., Ltd. (formerly Kyowa Hakko Kirin Co., Ltd. (KHK)) and UGNX entered into a Collaboration and License Agreement relating to the Product (as defined below) dated 29 August 2013, as amended, (the "**Collaboration Agreement**") under which KHK and UGNX have been collaborating on the development and commercialisation of the Product.

(B) KHK has licensed the right to develop, register and commercialise the Product in the Territory (as defined below) to UGNX.

(C) Kyowa Kirin has initiated commercial supply of Product including in the United States and the European Union (EU).

(D) UGNX wishes to make use of the Kyowa Kirin commercial supply capabilities for UGNX supply of Commercial Product in the Territory and Kyowa Kirin has agreed to this on the terms and conditions of this Agreement and in consideration of them.

(E) Kyowa Kirin and UGNX entered into an Early Access Supply Agreement dated 12 March 2018 (as amended and restated 15 November 2018) (the **"EAP Agreement"**) for Early Access Programme supply of the Product in the Territory.

THE PARTIES THEREFORE AGREE AS FOLLOWS:

1 DEFINITIONS

1.1 In this Agreement, the following words and expressions have the following meanings:

Affiliate	a person or entity that directly or indirectly Controls, is Controlled by, or is under common Control with the person or entity specified;
Agreed Supply Price	(a) thirty-five percent (35%) of Net Sales for Product sold in the Territory prior to January 1, 2023 and (b) thirty percent (30%) of Net Sales for Product sold in the Territory thereafter;
Anti-Bribery Law	all Applicable Laws addressing public corruption or commercial bribery whether in the Territory or otherwise;

Applicable Laws	all national, supranational, foreign or local laws (including case law), legislation, statutes, statutory instruments, rules, regulations, edicts, by-laws or directions or guidance from government or governmental agencies including any rules, regulations, guidelines or other requirements of relevant regulatory authorities which have the force of law;
Associated Person	has the meaning set out in Clause 17.2(a);
Batch Documentation	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 drug substance and drug product Batch records, laboratory control results and in-process control results, any applicable Deviation and investigation reports and the Certificate of Analysis, Certificate of Compliance, Change requests, which are required to comply with all applicable cGMP requirements;
Bribery Offence	has the meaning set out in Clause 17.1(a);
Business Day	any day which is not a Saturday, a Sunday or a bank or public holiday in the United States of America;
Chairman	has the meaning set out in Clause 28.4; has the meaning set out in Background (A).
Collaboration Agreement	
Commencement Date	November 02, 2020;
Commercially Reasonable Efforts	with respect to the development, manufacture or commercialisation of the Product, conducting such tasks using such efforts and resources that are typically used by a pharmaceutical company in conducting the same tasks on its own orphan or rare disease compounds or products with similar commercial and scientific potential at a similar stage in their lifecycle and in a similar therapeutic area, taking into consideration [***] and all other factors that are typically taken into consideration by pharmaceutical companies when determining

	the level of efforts and resources to apply to such tasks with respect to its own orphan or rare disease similar compounds or products (as described above). Commercially Reasonable Efforts shall be determined with respect to [***];
Confidential Information	the provisions of this Agreement and all information which is secret or otherwise not publicly available (in both cases either in its entirety or in part) including commercial, financial, marketing or technical information, know-how, trade secrets or business methods, or Data, in all cases whether disclosed orally or in writing before or after the date of this Agreement;
Control	that a person (i) possesses, directly or indirectly, the power to direct or cause the direction of the management and policies of the other Person (whether through the ownership of voting shares or power, ability to appoint directors, by contract or otherwise) or (ii) owns directly or indirectly, fifty percent (50%) or more of the voting securities or other ownership interest of the other Person. For purposes of this definition, “Person” means an individual, a corporation or a partnership. "Controls" and "Controlled" shall be interpreted accordingly;
Dispute	has the meaning set out in Clause 28.1;
Early Access Programme or EAP	a mechanism that enables patients with an unmet medical need to be provided with access to a medicine, prior to it being made commercially available in that country. Dependent upon national regulation, Early Access Programmes may encompass Early Access to Medicines Schemes (EAMS), Authorisation for Temporary Utilisation (ATU), Compassionate Use Programmes (CUP) and Named Patient Programmes (NPP). has the meaning set out in Clause 6.7;
Fixed Forecast Period	
For-Cause Audit	an audit of manufacturing records of Kyowa Kirin or its subcontractors, and/or an inspection of Kyowa Kirin’s manufacturing facilities, following: (a) an unfavorable critical observation during an inspection of a Public Authority that is potentially material to the quality of the Product or (b) a major or repeated quality excursion that may result in a failed Product batch or Product recall.

Force Majeure	any event outside the reasonable control of either party affecting its ability to perform any of its obligations (other than payment) under this Agreement including act of God, fire, flood, lightning, war, revolution, act of terrorism, riot, epidemic/pandemic, or civil commotion;
Good Distribution Practice	a set of criteria to be satisfied for the proper distribution of medicinal products for human use. It regulates the division and movement of products from the premises of the manufacturer or another central point, to the end user thereof, or to an intermediate point by means of various transport methods and also includes requirements for the purchase, receiving, storage, and export of drugs;
Good Manufacturing Practices	the good manufacturing practices required by the United States Food and Drug Administration and as set forth in the laws and regulations in the United States with respect thereto, for the manufacture and testing of pharmaceutical materials, and comparable Applicable Laws and requirements of Regulatory Authorities applicable to the manufacture and testing of pharmaceutical materials in jurisdictions within the Territory, as they may be updated from time to time, including applicable rules and guidelines promulgated under the International Conference on Harmonization;
Government Official	any officer, employee, agent or representative of any Public Authority (including any medical care provider controlled or funded in whole or in part by any Public Authority) or any political party, political party official or candidate for political office;
Healthcare Provider	an individual physician or other medical professional, a healthcare institution, or an administrator or any other person affiliated with a healthcare institution who may have influence on the decision to purchase, prescribe or use a Product;
Health Registration Approval	any and all approvals, licences, registrations or authorisations necessary to import, store, commercially distribute, sell and market the Product in the Territory, including, where applicable, (a) the MA, (b) pricing or reimbursement approval, and (c) labelling approval;
ICC	has the meaning set out in Clause 28.3;
Insolvency Event	where a party:

(a)

files for protection under bankruptcy or insolvency laws;

(b)

makes an assignment for the benefit of creditors;

(c)

appoints or suffers appointment of a receiver or an administrative receiver of, or an encumbrancer taking possession of or selling, the whole of or any part of the entity's undertaking, assets, rights or revenue;

(d)

proposes a written agreement of composition or extension of its debts;

(e)

proposes or is a party to any dissolution or liquidation;

(f)

files a petition under any bankruptcy or insolvency act or has any such petition filed against that is not discharged within sixty (60) days of the filing thereof;

(g)

admits in writing its inability generally to meet its obligations as they fall due in the general course; or

(h) suffers an event or is the subject of a proceeding in any jurisdiction to which it is subject that has an effect equivalent or similar to any of the events listed in points (a) to (g) above;

Intellectual Property Rights any patent, copyright, trade mark, service mark or trade name, utility model, right in software, right in design, right in databases, image right, moral right, right in an invention, right relating to passing off, domain name, right in confidential information (including trade secrets) or right of privacy, and all similar or equivalent rights in each case whether registered or not and including all applications (or rights to apply) for, or renewal or extension of, such rights which exist now or which will exist in the future in the Territory and all other countries in the world;

Inventory Acceptance Requirements the following standard inventory acceptance requirements:

(a) minimum shelf life as set out in Clause 6.4;

(b) compliance with the Quality Agreement;

(c) compliance with the Product specifications contained in the relevant MA; and

(d) compliance with Good Manufacturing Practices;

KHK	Kyowa Kirin Co., Ltd. (formerly Kyowa Hakko Kirin Co., Ltd);
Losses	has the meaning set out in Clause 20.1;
MA	a Marketing Authorization to sell a pharmaceutical product in any country in the Territory;
Minimum Order Quantity	has the meaning set out in Clause 6.16;
Minimum Supply Price	[***] US Dollars ($[***) per vial of Product.
Net Sales	has the meaning set out in Schedule 1 (Price and Payment);
Out of Condition	Kyowa Kirin Product that is not in compliance with Applicable Laws, Good Distribution Practices, Good Manufacturing Practices or instructions from Kyowa Kirin;
Personnel	the employees of or persons otherwise engaged by UGNX for the purpose of fulfilling this Agreement;
Product	KHK's recombinant human IgG1 monoclonal antibody product targeting FGF23 identified as KRN23 (burosumab solution for injection bulk naked vials in 10mg, 20mg and 30mg presentations);
Profit Share Territory	has the meaning ascribed to it in the Collaboration Agreement;
Public Authority	any national, subnational or local government or any subdivision, authority or agency thereof;
Purchase Order Lead Time	has the meaning set out in Clause 6.14;
Quarter	one of the three month periods ending upon 31st March, 30th June, 30th September and 31st December in each Year during the term of this Agreement, [***] until the date on which this Agreement expires or is terminated;

[***] Report	has the meaning set out in Schedule 1 (Price and Payment);
Rules	has the meaning set out in Clause 28.3;
Quality Agreement	the agreement to be entered into between Kyowa Kirin and UGNX, defining the roles and responsibilities for each party in relation to the quality and manufacture of the Product in the Territory;
Term	the term of this Agreement as set out in Clause 2.1;
Termination	the termination or expiration of all or part of this Agreement;
Termination Date	the date on which Termination takes effect;
Territory	On a country-by-country basis, upon Health Registration Approval following which such country ceases to be part of the territory under the EAP Agreement, Argentina, Brazil, Chile, Colombia, Mexico, Peru, Ecuador, Costa Rica, Guatemala, El Salvador, Honduras, Belize and Panama;
The Kyowa Kirin Indemnified Party	has the meaning set out in Clause 20.1;
The UGNX Indemnified Party	has the meaning set out in Clause 20.2;
Tribunal	has the meaning set out in Clause 28.4;
Withholding Tax	has the meaning set out in Clause 10.6;
Year	a period of twelve (12) months commencing on the Commencement Date and on each successive anniversary of the Commencement Date and ending on the day before each successive anniversary of the Commencement Date;

1.2 Drafting Conventions

(a) The headings in this Agreement are inserted for convenience only and shall not affect the interpretation or construction of this Agreement.

(b) Words expressed in the singular shall include the plural and vice versa. Words referring to a particular gender include every gender. References to a person include an individual, company, body corporate, corporation, unincorporated association, firm, partnership or other legal entity.

(c) The words "other", "including" and "in particular" shall not limit the generality of any preceding words or be construed as being limited to the same class as any preceding words where a wider construction is possible.

(d) References to any statute or statutory provision shall include (i) any subordinate legislation made under it, (ii) any provision which it has modified or re-enacted (whether with or without modification), and (iii) any provision which subsequently supersedes it or re-enacts it (whether with or without modification) whether made before or after the date of this Agreement.

(e) All references in this Agreement to Clauses, and Schedules are to the clauses, and schedules to this Agreement unless otherwise stated.

2 DURATION

2.1 This Agreement shall come into force on the Commencement Date and shall, subject to the provisions for earlier termination set out in this Agreement, continue in force throughout the term of the Collaboration Agreement, and thereafter this Agreement shall be automatically extended for consecutive [***] periods unless either party gives [***] written notice of termination to terminate at the date of expiration of the Collaboration Agreement or at the end of any subsequent renewal period (the "**Term**"), or unless both parties mutually agree to a termination date in writing.

3 APPOINTMENT

3.1 UGNX hereby appoints Kyowa Kirin and Kyowa Kirin hereby accepts the appointment as UGNX's exclusive supplier of the Product for commercialisation in the Territory subject to and in accordance with the provisions of this Agreement.

4 EXCLUSIVITY

4.1 Throughout the Term of this Agreement:

(a) Kyowa Kirin shall exclusively supply UGNX with the Product in the Territory. This means that Kyowa Kirin shall not be entitled to appoint other distributors in the Territory, actively sell or distribute, nor permit the distribution of the Product directly to customers in the Territory; and

(b) UGNX shall exclusively purchase its supplies of the Product in the Territory from Kyowa Kirin. This means UGNX shall not purchase supplies of the Product from any other party for resale to customers in the Territory.

5 APPROVALS, AUTHORISATIONS, PRICING AND REIMBURSEMENT

5.1 Following grant of an MA for the Product in each country in the Territory, UGNX (or its designee) shall maintain the MA, including carrying out, in a timely manner, [***] expense, any necessary regulatory variation required following notification by Kyowa Kirin of any change to the Product specification, which change Kyowa Kirin shall notify to UGNX as soon

as reasonably practicable. Kyowa Kirin shall provide to UGNX all necessary documentation, expertise and know-how for the maintenance of the MAs, including without limitation, any necessary regulatory variation, as further set forth in the Quality Agreement and/or as reasonably requested by UGNX.

5.2 During the Term of this Agreement UGNX shall be solely responsible for any necessary negotiation of pricing and reimbursement for the Product in the Territory.

5.3 During the Term of this Agreement UGNX shall have sole responsibility for seeking, obtaining and maintaining all licenses, registrations, permits and Health Registration Approvals, and for market access, distribution, medical affairs, and pharmacovigilance for the Product (subject to the pharmacovigilance agreement between the parties in respect of the Product in the Territory).

5.4 In the event of changes to facilities, equipment, processes, specifications, quality control and sourcing of material, sampling and test methods and quality assurance release process, both parties shall use their [***] to minimize obsolescence and interruption of supply. The change-initiating party shall notify the other party as soon as practicable of the planned change. UGNX is responsible to approve and determine the regulatory impact of such change in the Territory. Kyowa Kirin shall provide to UGNX an inventory reconciliation of such materials with [***] of notification by either party of the planned change. The parties shall mutually agree upon an implementation schedule for the planned change and means to minimize obsolescence and interruption of supply. The party initiating the changes shall be responsible [***] associated with the resulting obsolescence.

6 SUPPLY OF PRODUCTS

Product Overview

6.1 During the Term of this Agreement, Kyowa Kirin shall supply Product as naked, unlabelled product. Product will be supplied to UGNX from the bulk drug Product supply maintained at Kyowa Kirin's packaging facility or its approved third party packaging facility as outlined in section 7.2. Kyowa Kirin agrees to maintain in inventory of sufficient Product, as mutually agreed through the joint sales and operations planning process.

6.2 Kyowa Kirin will manufacture and test the drug substance and drug product at manufacturing sites as approved in the Territory's Marketing Authorization. UGNX will have reasonable access to audit and oversee the drug substance and drug product manufacturing sites to support their compliance with UGNX MAs. Oversight rights and requirements will be subject to the Collaboration Agreement and the Quality Agreement.

6.3 Kyowa Kirin warrants that the Product supplied under this Agreement will, on the date of delivery and throughout the Product shelf-life, meet the Inventory Acceptance Requirements, Specification, and be manufactured in accordance with all Applicable Laws, provided that the Product has been stored and handled by Kyowa Kirin and

UGNX in accordance with Good Distribution Practice, relevant Product dossiers, and the Quality Agreement.

6.4 Product provided to UGNX shall have no less than [***] of remaining shelf life at the date of delivery to UGNX. Kyowa Kirin will [***] to maximize available shelf-life for UGNX upon delivery. Accommodation to accept material with [***], shall be worked on by both parties in good faith to optimize the total drug product inventory and reduce product expiry.

6.5 Subject to the terms of this Agreement and the requirements of Applicable Laws, Kyowa Kirin will retain all rights and responsibility to conduct at its cost all necessary development activities related to the manufacture and supply of the Product, including process development, manufacturing scale-up, development-stage and commercial- stage manufacturing, quality assurance/quality control procedure development, and compilation and reporting of CMC (Chemistry, Manufacturing Controls) information.

Rolling Forecasts

6.6 Upon Commencement Date or filing for product approval with the Health Authority in each country of the Territory, whichever occurs first, UGNX shall submit [***] forecasts. [***] during the Term of this Agreement, UGNX shall submit to Kyowa Kirin, within [***] after the [***] of each [***], written or electronic forecasts of the quantities on a rolling basis of the Product that it desires or expects to order from Kyowa Kirin during [***] period. Forecasts shall be [***] in the subsequent [***] period.

Firm Commitment and Estimates

6.7 The first [***] ("**Fixed Forecast Period**") covered by each forecast shall constitute a binding commitment by UGNX to purchase the quantities of Product covered by such forecast.

6.8 With respect to [***] of the forecast, quantities shall constitute a non-binding forecast of UGNX orders, presented solely for the purposes of [***].

6.9 Within [***] of start of Fixed Forecast Period, Kyowa Kirin shall confirm to UGNX the Product Batch information including lot number to allow UGNX to commence Batch Documentation review. Kyowa Kirin shall make available to UGNX all Batch Documentation necessary to support UGNX confirmation that the Product complies with the Inventory Acceptance Requirements. UGNX shall confirm to Kyowa Kirin suitability of the lot for the Territory or intended market within the Territory [***] of receipt of all Batch Documentation necessary to confirm conformance with Inventory Acceptance Criteria. In the event the lot is not deemed acceptable for the Territory, Kyowa Kirin shall [***].

6.10 After UGNX provides confirmation that the lot has met Inventory Acceptance Requirements, the Product shall remain [***] until delivery occurs in accordance with Clause 7.

6.11 UGNX shall from time to time submit a purchase order in a written form approved by Kyowa Kirin for the supply of Product in accordance with the forecast quantities in the Fixed Forecast Period described in Clause 6.7 above. UGNX shall place purchase orders [***]. The purchase order shall [***].

6.12 Printed or written purchase orders, order acknowledgements or invoices shall not modify or expand either party's obligations under this Agreement. In the event of any inconsistency between the terms of any purchase order, order acknowledgement or invoice, and the terms of this Agreement, the terms of this Agreement shall prevail.

Acceptance of Purchase Orders

6.13 Kyowa Kirin shall confirm receipt of a purchase order within [***] of receipt. Acceptance or rejection of a purchase order shall be made in writing, including by email, within [***] of receipt, with such acceptance of the order to include [***]; provided, however, in the event Kyowa Kirin does not [***], the applicable purchase order shall be deemed accepted. Kyowa Kirin may only reject a purchase order if that order:

(a) [***];

(b) [***];

(c) [***];

(d) [***]; or

(e) [***]

6.14 The purchase order lead time for the supply of the Product to UGNX shall be [***] (the "**Purchase Order Lead Time**").To the extent that any order provides for a due date that is less than the Purchase Order Lead Time, Kyowa Kirin shall be entitled to require that the due date be postponed in line with the Purchase Order Lead Time.

6.15 If Kyowa Kirin is unable to meet the requested due date or quantity of a purchase order, Kyowa Kirin shall notify UGNX within [***]. Kyowa Kirin will [***] to minimize the delay. To the extent the available supply of, or capacity to manufacture the Product is less than the requirements of UGNX and its Affiliates hereunder together with the requirements of Kyowa Kirin and its Affiliates and their licensees, Kyowa Kirin shall allocate the available Product [***]. In the event of any shortage in availability of supply of, or capacity to manufacture Product as contemplated by this Clause, the parties will [***]. Notwithstanding the foregoing, at the request of UGNX, if UGNX has met its obligations for Fixed Forecasts in Sections 6.7 – 6.10 above, [***] as a result of

[***]. If UGNX has not met its obligations for Fixed Forecasts then [***]. Kyowa Kirin agrees to maintain in inventory sufficient bulk drug substance for the Product, in line with the Product supply chain strategy as mutually agreed through the joint sales and operations planning process, based on UGNX's most recent forecast for the Territory.

Minimum Order Quantity and Deviation from Minimum Order Quantity

6.16 UGNX shall place orders for the Product based on a minimum order quantity of [***] ("**Minimum Order Quantity**"). Orders for the Product of quantities exceeding the Minimum Order Quantity shall be placed by UGNX in increments of the Minimum Order Quantity.

In the event that UGNX desires to purchase a quantity of Product which is less than the Minimum Order Quantity, then [***]. The parties shall work to achieve an order quantity and delivery methodology that is appropriate for both parties.

Regular Business Reviews

6.17 The parties shall nominate representatives who meet, either in person or by telephone or by video conference, as applicable, on a regular, at least [***], basis as necessary [***] to review manufacturing, forecasting, logistical and quality assurance aspects to resolve any pending issues in relation to such aspects. These regular business reviews may be part of the standing sales and operations planning (S&OP) meeting or the regular business reviews may be separate meetings.

7 DELIVERY AND ACCEPTANCE OF PRODUCT

7.1 Any dates specified by Kyowa Kirin for delivery of the Product are intended to [***] to ensure that delivery shall be within the Purchase Order Lead Time. If no dates are so specified, Kyowa Kirin shall [***] to ensure that delivery will be within the Purchase Order Lead Time.

7.2 Product will be delivered to UGNX by Kyowa Kirin [***] to regional packaging facility located in [***] or other such packaging facility as approved in advance by UGNX. Product shall be made available to UGNX from Kyowa Kirin approved inventory from a regional packaging facility, having already been transported from the point of manufacture to a regional packaging facility using Kyowa Kirin qualified shipping lanes.

7.3 All Product supplied by Kyowa Kirin shall be examined and checked upon transfer or delivery to UGNX (or its designee at the regional packaging site) in order to ascertain that the Product complies with the lot release information, quantity, and Inventory Acceptance Requirements.

7.4 Unless Kyowa Kirin is notified in writing within [***] after the date of delivery, of (i) any non-compliance with the lot release information, quantity, or

Inventory Acceptance Requirements which can be reasonably detected through visual inspection of the Product or (ii) any alleged shortages in the quantity of delivered Product, [***]. In the event that UGNX determines [***] after the date of delivery, that the Product did not materially conform with the specifications on the date of delivery or otherwise comply with the product warranty in Clause 6.3 or the requirements of the purchase order (such as matching the quantities ordered), UGNX shall provide notice to Kyowa Kirin thereof, and, if requested by Kyowa Kirin, ship or provide a sample portion of the affected Product to Kyowa Kirin or its designated contract manufacturing organization (CMO), freight prepaid and properly insured, along with a reasonably detailed statement of the claimed non-conformity and copy of Kyowa Kirin's invoice therefor. UGNX shall retain the balance of the Product that is subject to review subject to resolution of the rejection and further disposition in accordance with this Clause 7.

7.5 For quality defects which are not reasonably detectable through visual inspection, UGNX shall notify Kyowa Kirin thereof by written notice within [***] after becoming aware thereof. In case of non-compliance with the Inventory Acceptance Requirements and UGNX notifies Kyowa Kirin of such non-compliance in accordance with this Clause 7.5, Kyowa Kirin shall, at Kyowa Kirin's option, either replace such Product [***] or refund [***] as soon as reasonably feasible.

7.6 In the event that Kyowa Kirin agrees that the returned Products were non-conforming (or such non-conformance is confirmed under Clause 7.7 below), Kyowa Kirin shall replace all of such non-conforming units of Product, [***], and Kyowa Kirin shall as soon as practicable deliver to UGNX, freight prepaid, all replacement units of the Product, [***]. UGNX shall return all non-conforming Product to Kyowa Kirin per instructions provided [***].

7.7 In the event that Kyowa Kirin disagrees with UGNX's rejection because the Product is in fact conforming, the parties shall cooperate to have both UGNX's returned samples and Kyowa Kirin's retained samples from the same production batch of the Product in dispute analyzed by a mutually acceptable independent testing laboratory of recognized reputation in the pharmaceutical industry, using the analytical methods, tests and criteria for conformance set forth in the specifications. If Kyowa Kirin is unable to deliver the Product on time because UGNX has not provided appropriate instructions, documents, licences or authorisations, then the Product will be deemed to have been delivered, [***] and Kyowa Kirin may store the Product, in conditions which adequately protect and preserve the Product, until actual date of delivery, [***].

7.8 The up-front out-of-pocket external costs associated with the return in 7.7 shall be [***] by the parties, unless and until an alternative determination is made as provided below. The results of such laboratory testing shall be conclusive and binding on the parties on the issue of compliance of such units of Product with the specifications on the date of delivery. If such independent testing laboratory determines that UGNX's returned samples of such Product conform to the specifications and other Product warranties hereunder, then (i) the applicable Product shall be deemed to have been improperly rejected by UGNX, and (ii) [***]. If such independent testing laboratory determines that UGNX's returned samples of such Product did not

conform to the specifications and other Product warranties hereunder and that such returned samples conform to the samples for such batch retained by Kyowa Kirin, then [***], and Kyowa Kirin shall promptly supply to UGNX conforming Product in accordance with Clause 7.6.

7.9 UGNX will provide, [***], at the place of delivery or transfer, adequate and appropriate equipment and manual labor for acceptance and receipt of the Product.

7.10 In the event that the quantities of the Product delivered to UGNX (in one or more shipments) do not match the quantity ordered in any material respect, Kyowa Kirin shall promptly ship (such shipping at [***]) the additional Product required to make up such shortfall; or if the amount shipped exceeds the amount ordered by a material amount, UGNX shall accept only the amount ordered, in which case upon Kyowa Kirin's request and at [***], such additional quantities shall be returned to Kyowa Kirin or stored by UGNX [***].

8 RISK AND TITLE

8.1 Title and risk of loss to Products shall pass to UGNX upon transfer or delivery to UGNX or its designee.

9 PRODUCT SAFETY, RETURN AND RECALL

9.1 Prior to the first supply of the Product, the parties shall agree and execute:

(a) the Quality Agreement; and

(b) a form of pharmacovigilance agreement.

9.2 Each party shall comply at all times with the written instructions and all written guidelines issued from time to time attached to the Product concerning their storage, application and use (including as set out in the Quality Agreement) and each party shall refer its Personnel and customers to such instructions, guidelines and the Quality Agreement.

9.3 Each party shall keep the other properly informed of all customer complaints concerning the Product and shall comply with any reasonable directions of the other party in any issues, proceedings or negotiations relating to such complaint, subject to compliance with Applicable Laws.

9.4 If any used Product is returned to UGNX for any reason other than Product quality claims, UGNX shall promptly notify Kyowa Kirin and if requested shall ship such Product to Kyowa Kirin [***] of the return, unless Applicable Law prohibits such shipment. Kyowa Kirin shall [***].

9.5 If Kyowa Kirin notifies UGNX in writing of any defect in the Product previously delivered by Kyowa Kirin or any error or omission in the instructions for the use of the Product which exposes or may expose consumers to any risk of death, injury or damage to property, UGNX shall [***] under this section.

9.6 UGNX is responsible for determination of need for recall, withdrawal, or field corrections in the Territory. UGNX and Kyowa Kirin shall [***] notify each other of any recall or potential recall of the Product. Without prejudice to the terms of the Quality Agreement, Kyowa Kirin may, at its discretion [***], determine a need to recall Product sold or allocated to UGNX. Kyowa Kirin shall [***] for any such recalled Product and/or resupply conforming Product to UGNX [***].

10 PRICE AND PAYMENT

10.1 UGNX shall pay to Kyowa Kirin the applicable payments in relation to the supply of the Product in accordance with the provisions of Schedule 1.

10.2 All sums payable under this Agreement are [***] of VAT or any other applicable tax or duty that must be paid in addition at the rate and in the manner prevailing at the relevant tax point.

10.3 All amounts to be paid by the parties under this Agreement shall be in US Dollars and payment shall be in US Dollars by electronic transfer to the bank accounts as notified by the parties from time to time with any applicable charges on such payments being at the recipient's expense.

10.4 Without prejudice to Clause 10.5, if any undisputed sum due from UGNX to Kyowa Kirin under the Agreement is not paid on or before the due date for payment and not cured within [***] following UGNX's receipt of written notice thereof, then without prejudice to Kyowa Kirin's other rights under this Agreement, Kyowa Kirin shall be entitled to:

(a) [***];

(b) [***]; and

(c) [***].

10.5 If any sum payable under this Agreement is not paid when due such non-payment is and not cured within [***] following the defaulting party's receipt of written notice thereof then, without prejudice to the non-defaulting party's other rights under this Agreement, it shall be entitled to charge interest on the overdue amount from the due date until payment is made in full both before and after any judgment, [***].

10.6 A party receiving a payment pursuant to this Agreement shall [***] taxes levied on such payment. If a party making payment is required under Applicable Laws to pay any withholding tax, charge, or levy ("**Withholding Tax**") in respect of any payments due under the Agreement, the remitting party shall:

(a) [***] from the payment;

(b) make [***] to the proper governmental authority for the account of the other party; and

(c) provide the other party with [***].

To the extent that amounts [***].

10.7 The parties acknowledge and agree that (a) KHK is responsible for all third party royalties under the Collaboration Agreement and (b) UGNX shall have no obligation to pay royalties to any third party under this Agreement.

11 KYOWA KIRIN'S UNDERTAKINGS

11.1 Kyowa Kirin agrees that at all times during the Term of this Agreement it shall:

(a) promptly inform UGNX of any changes in the specifications of the Product (which may not occur without UGNX's prior approval, not to be unreasonably withheld) or of the discontinuation of production of any of the Product, whenever reasonably possible;

(b) shall supply the Product to UGNX for sale in the Territory in accordance with UGNX's forecast requirements, this Agreement and the Quality Agreement; and

(c) comply with all Applicable Laws.

12 UGNX OBLIGATIONS

12.1 UGNX shall during the Term of this Agreement:

(a) use [***] to hold stocks of Product sufficient to meet reasonably anticipated demand for the Product from the customers in the Territory;

(b) at [***] (except as otherwise expressly set forth in this Agreement) ensure that any registration, translation, labelling or warning or notification requirements concerning this Agreement or the Product are in accordance with all Applicable Laws and UGNX shall promptly provide full details of all actions taken in this respect to Kyowa Kirin;

(c) employ sufficient and suitable Personnel to perform its obligations under this and the Quality Agreement and ensure that all such Personnel are appropriately trained to perform such obligations;

(d) if Product in the possession of, under the control of or sold by UGNX is or becomes Out of Condition UGNX shall, if required by Kyowa Kirin, give all reasonable assistance to Kyowa Kirin in locating and recovering the Out of Condition Product and preventing its sale to third parties;

(e) comply with all Applicable Laws and manage all contacts with regulatory authorities and Healthcare Providers in the Territory, including all registrations for the lawful sale of the Product;

(f) be responsible for seeking, obtaining and maintaining all licenses, registrations, permits and Health Registration Approvals required to be obtained by UGNX to enable UGNX to act as distributor and importer of the Product in the Territory pursuant to this Agreement;

(g) be responsible for all customs, duties and other governmental charges relating to the importation of the Product in the Territory;

(h) be responsible for all quality control release testing, retention of samples, lot release, labelling and packaging of the Product for commercial distribution in the Territory, all in full compliance with the Applicable Laws; and

(i) for a period of [***], or longer if required by Applicable Laws, store and make available to Kyowa Kirin the following information:

(i) [***]; and

(ii) [***].

13 COMPLIANCE WITH LAWS AND REGULATIONS

13.1 UGNX shall [***] to give Kyowa Kirin [***] of any prospective changes in any Applicable Laws in the Territory of which UGNX is aware and which, to the knowledge of UGNX may affect the manufacturing Kyowa Kirin's manufacturing responsibility requirements of the Product as sold into the Territory.

13.2 On receipt of notification from UGNX under Clause 13.1, Kyowa Kirin shall [***] to ensure that the Product complies with any change in the Applicable Laws by the date of implementation of that change or as soon as is reasonably possible afterwards.

14 RECORD KEEPING AND COOPERATION WITH INSPECTION

14.1 UGNX shall maintain complete and accurate records concerning:

(a) all of its purchases and sales of the commercial product derived from the naked unlabelled vials of Product;

(b) records related to its quality and regulatory obligations under this Agreement. UGNX shall maintain quality and regulatory records in an orderly fashion for a period of [***] counting from the date of each purchase or sale. UGNX shall, at Kyowa Kirin's request made upon reasonable notice (such notice to be presumed reasonable if made at least [***] in advance [***]) during normal business hours, in such a way as not to disrupt normal business, and [***], provide Kyowa Kirin (or its designated representative) with [***] access to all records required by this Clause 14.1 at UGNX's place of business or at such other location mutually agreed upon by the parties, and shall fully cooperate in allowing Kyowa Kirin (or its designated representative) to inspect such records as requested, under confidentiality obligations. To enable Kyowa Kirin to conduct such inspection in a non-invasive manner, UGNX shall [***].

UGNX shall notify Kyowa Kirin of filing for regulatory approval in a country in the Territory within [***] of submission of filing, such that Kyowa Kirin can prepare for any related inspection by a health authority or other regulatory body.

14.2 Kyowa Kirin shall advise UGNX promptly, but in no event later than [***] after Kyowa Kirin's receipt of notice thereof, of any planned regulatory authority visit to the portion of the facilities of Kyowa Kirin or its Affiliates or CMO where Product is manufactured, stored or handled or any material written inquiries by a regulatory authority concerning such facilities, the procedures of Kyowa Kirin or its Affiliates or CMO for the manufacture, storage or handling of Product. If the regulatory authority makes an unannounced or unplanned visit, or if Kyowa Kirin does not have at least [***'] notice of the visit, Kyowa Kirin shall inform UGNX of the visit within [***] after Kyowa Kirin obtains actual knowledge of the visit. Kyowa Kirin shall inform UGNX as soon as practicable regarding the purpose and result of such visit or inquiry, and shall provide to UGNX [***], to the regulatory authority or issued by or provided by the regulatory authority to Kyowa Kirin or its Affiliates or CMO, as the case may be, in connection with such visit or inquiry.

15 REPORTING PROCEDURE

15.1 UGNX shall promptly (or as otherwise set forth herein) notify Kyowa Kirin of:

(a) on a [***] basis, all material enquiries concerning the Product or orders for the Product that it receives and respond as instructed by Kyowa Kirin;

(b) any material non-compliance observations or complaints made by customers in respect of the Product , and, insofar as the compliant relates to the Product itself, shall not, [***]; and

(c) any actual, threatened or suspected infringement by the Product of any Intellectual Property Rights belonging to any third party or any actual, threatened or suspected infringement by any third party of the Intellectual Property in the Product which comes to UGNX's notice from time to time and [***] to safeguard the property rights and interests of Kyowa Kirin and [***].

15.2 Both parties understand and agree to comply with all applicable domestic and foreign financial transparency/disclosure laws and other associated rules and regulations. Each party shall manage its own records and independently report to the appropriate governmental agency(s).

16 DATA PROTECTION

16.1 Sensitive personal data and processing shall be managed according to the Applicable Laws in each of the Territory.

17 ANTI BRIBERY

17.1 Each party warrants and represents to the other party that it:

(a) has not committed an offence under any Anti-Bribery Law (a "**Bribery Offence**");

(b) has not been formally notified that it is subject to an investigation relating to alleged Bribery Offences or prosecution or enforcement action under any Anti- Bribery Law;

(c) is not aware of any circumstances that could give rise to an investigation relating to an alleged Bribery Offence or prosecution or enforcement action under any Anti-Bribery Law.

17.2 Each party agrees that it:

(a) has in place, and shall maintain until termination of this Agreement, adequate documented procedures designed to prevent persons associated with such party (including an employee, sub-contractor or agent or other third party working on behalf of such party or any Affiliate) (an "**Associated Person**") from committing a Bribery Offence; and

(b) shall comply with any applicable Anti-Bribery Law and shall not, and shall procure that no Associated Person shall, commit any Bribery Offence or any act which would constitute a Bribery Offence; and

(c) comply with all compliance requirements and related operating procedures, direction and guidance for interaction with Healthcare Providers or Government Officials;

(d) shall not do or permit anything to be done which would cause the other party or any of the other party's employees, sub-contractors or agents to commit a Bribery Offence or incur any liability in relation to an act of bribery; and

(e) shall not, directly or indirectly, make offer, promise, or authorise the payment or giving of any money or thing of value to any third party (which includes a Government Official or any Healthcare Provider or other person) for the purpose of obtaining any improper business advantage. Such purpose shall be deemed to exist if a payment or gift is made, offered, promised or authorized with the intent to or with the knowledge that it is likely to:

> (i) corruptly affect or influence any act or decision of a third party, including a decision to fail to perform his or her lawful duty; or
>
> (ii) induce a third party to corruptly affect or influence any act or decision of any Public Authority or customer in order to assist Kyowa Kirin or UGNX in connection with the use or sale of the Product; and

(f) shall notify the other party, to the extent legally practicable and permissible, immediately in writing if it becomes aware or has reason to believe that it has, or any of its Associated Persons have, breached or potentially breached any of the party's obligations under this Clause 17. Such notice to set out full details, to the extent legally practicable and permissible under Applicable Laws and

Confidentiality obligations, of the circumstances concerning the breach or potential breach of such party's obligations.

17.3 Each party acknowledges that no employee of the other party or any of its Affiliates has any authority to give any direction, written or oral, in contravention of the foregoing in connection with the making of any payment or commitment by the party to any third party.

17.4 Each party acknowledges that the failure of itself, its employees, agents, sub- distributors or other representatives to comply strictly with this Clause 17 shall be considered, if proven that a breach of this Clause 17 was actually committed, a material breach of this Agreement and the other party shall be entitled to terminate the Agreement in accordance with Clause 22.1. In addition, such failure may subject the other party and its Affiliates, employees, agents and other representatives to substantial fines, penalties, damages, expenses, the imposition of additional taxes or the loss of tax deductions.

18 FORCE MAJEURE

18.1 A party will not be in breach of this Agreement nor liable for any failure or delay in performance of any obligations under this Agreement (and the date for performance of the obligations affected will be extended accordingly) as a result of Force Majeure, provided that such party complies with the obligations set out in this Clause 18 (Force Majeure). Save as provided in Clause 18.4, a Force Majeure will not entitle either party to terminate this Agreement.

18.2 The party affected by Force Majeure shall immediately notify the other in writing of the matters constituting the Force Majeure and shall keep that party fully informed of their continuance and of any relevant change of circumstances whilst such Force Majeure continues.

18.3 The party affected by Force Majeure shall take all reasonable steps available to it to minimise its effects on the performance of its obligations under this Agreement.

18.4 If Force Majeure continues for longer than [***] either party may, whilst the Force Majeure continues, immediately terminate this Agreement by notice in writing to the other.

19 LIABILITY

19.1 Nothing in this Agreement excludes or limits either party's liability for:

(a) [***];

(b) [***]; or

(c) any liability that cannot legally be excluded or limited.

19.2 Subject to Clause 19.1, each party is not liable, whether in contract, tort (including negligence or breach of statutory duty), misrepresentation or otherwise in connection with this Agreement for any*:*

(a) [***];

(b) [***];

(c) [***]; or

(d) [***];

in each case whether direct or indirect, or for any indirect, special or consequential loss or damage, howsoever arising.

20 INDEMNITY

20.1 Indemnification by UGNX: UGNX shall indemnify, defend and hold harmless Kyowa Kirin, its Affiliates, and its and their respective, directors, officers and employees (collectively "**the Kyowa Kirin Indemnified Party**") against any and all claims, liabilities, losses, damages, costs or expenses, including reasonable attorneys' fees, arising out of any claim or action brought by a third party (collectively, "**Losses**") incurred or suffered by the Kyowa Kirin Indemnified Party to the extent arising out of or caused by:

(a) the negligence, recklessness or intentional misconduct of UGNX or its Affiliates in connection with the importation, storage, sale, offer for sale and distribution of the Product in the Territory; or

(b) the breach by UGNX of one or more of its representations, warranties or other material obligations under this Agreement,

except to the extent such Losses result from or arise out of (i) the inaccuracy of any representation of warranty of Kyowa Kirin set forth in this Agreement; (ii) the breach of any warranty or covenant contained in this Agreement by Kyowa Kirin; or (iii) the negligence, recklessness or intentional misconduct of Kyowa Kirin.

20.2 Indemnification by Kyowa Kirin: Kyowa Kirin shall indemnify, defend and hold harmless UGNX, its Affiliates, and its and their respective, directors, officers and, employees (collectively "**the UGNX Indemnified Party**") against any and all Losses (as defined above) incurred or suffered by the UGNX Indemnified Party to the extent arising out of or caused by:

(a) the negligence, recklessness or intentional misconduct of Kyowa Kirin or its Affiliates in connection with the manufacturing, quality control, release and supply of the Product;

(b) a deficiency in the Product, provided that this shall not extend to any Loss arising out of or related to (i) [***], or (ii) [***];

(c) the breach by Kyowa Kirin of one or more of its representations, warranties or other material obligations under this Agreement; or

(d) any infringement claim made, brought or threatened against UGNX as a result of an alleged or actual infringement of a third party's Intellectual Property Right, to the extent such infringement claim (and related Losses) arises out of UGNX's importation, storage, sale, offer for sale, distribution, marketing, use, or promotion of the Product in the Territory in accordance with the MA,

except to the extent such Losses result from or arise out of (i) the inaccuracy of any representation of warranty of UGNX set forth in this Agreement; (ii) the breach of any warranty or covenant contained in this Agreement by UGNX; or (iii) the negligence, recklessness or intentional misconduct of UGNX.

20.3 Notification of Liabilities/Losses: In the event that either party intends to seek indemnification for any claim under any of Clauses 20.1 or 20.2, it shall inform the other party of the claim promptly after receiving notice of the claim.

20.4 In the case of a claim for which Kyowa Kirin seeks indemnification under Clause 20.1, upon UGNX's request, Kyowa Kirin shall permit UGNX to direct and control the defence of any claim and shall provide such reasonable assistance as is reasonably requested by UGNX (at UGNX's cost) in the defence of the claim; provided that nothing in this Clause 20.4 shall permit UGNX to make any admission on behalf of Kyowa Kirin, or to settle any claim or litigation which would impose any financial obligations on Kyowa Kirin without the prior written consent of Kyowa Kirin, such consent not to be unreasonably withheld or delayed. Notwithstanding the foregoing, Kyowa Kirin may participate at its own expense in the defense and any settlement discussions.

20.5 In the case of a claim for which UGNX seeks indemnification under Clause 20.2, upon Kyowa Kirin's request, UGNX shall permit Kyowa Kirin to direct and control the defence of the claim and shall provide such reasonable assistance as is reasonably requested by Kyowa Kirin (at Kyowa Kirin's cost) in the defence of the claim, provided always that nothing in this Clause 20.5 shall permit Kyowa Kirin to make any admission on behalf of UGNX, or to settle any claim or litigation which would impose any financial obligations on UGNX without the prior written consent of UGNX, such consent not to be unreasonably withheld or delayed. Notwithstanding the foregoing, UGNX may participate at its own expense in the defense and any settlement discussions.

20.6 Neither party limits or excluded its liability for fraudulent misrepresentation nor for death or personal injury arising from its negligence.

20.7 Exclusive Remedy: Each party agrees that its sole and exclusive remedy with respect to any Losses shall be pursuant to the indemnification provision of this Clause 20. For clarity, no remedies with respect to claims or losses other than Losses shall be limited by this Clause 20.7.

21 INSURANCE

21.1 UGNX and Kyowa Kirin shall maintain sufficient insurances with reputable providers to cover any and all liabilities arising out of or in connection with this Agreement, including [***].

22 TERMINATION

22.1 If the Collaboration Agreement is terminated, either party may immediately terminate this Agreement without payment of compensation of other damages caused to the other party solely by such termination by giving notice in writing to the other party. Notwithstanding any other provision, all amounts payable to Kyowa Kirin under the Agreement shall remain due upon termination of this Agreement for whatever reason pursuant to the payment terms set forth herein.

22.2 It is expressly agreed that, to the maximum extent permitted by the laws within the Territory, termination of this Agreement (in accordance with the terms of this Agreement) at any time and for whatever reason shall not entitle [***] in accordance with or in relation to this Agreement.

23 CONSEQUENCES OF TERMINATION

23.1 The Termination of this Agreement will be without prejudice to the rights and remedies of

either party that may have accrued up to the date of termination.

23.2 On Termination of this Agreement for any reason whatsoever:

(a) subject to Clause 23.1, the relationship of the parties will cease and any rights or licences granted under or pursuant to this Agreement will cease to have effect save as (and to the extent) expressly provided for in this Clause 23;

(b) any provision which expressly or by implication is intended to come into or remain in force on or after termination will continue in full force and effect;

(c) subject to Clause 23.2(d) each of the parties shall immediately return to the other party (or, if the other party so requests by notice in writing, destroy) all of the other party's property in its possession at the date of termination, including all of its Confidential Information, together with all copies of such Confidential Information and shall certify that it has done so, and shall make no further use of such Confidential Information; and

(d) if a party is required by any Applicable Laws, regulation or government or regulatory body to retain any documents or materials which it would otherwise be required to return or destroy by Clause 23.2(c), it shall notify the other party in writing of such retention, giving details of the documents or materials that it must retain; and

24 CONFIDENTIALITY

24.1 Each party shall keep and procure to be kept secret and confidential all Confidential Information belonging to the other party disclosed or obtained as a result of the relationship of the parties under this Agreement and shall not use nor disclose the same save for the purposes of the proper performance of this Agreement or with the prior written consent of the other party.

24.2 The parties may disclose Confidential Information to an employee, Affiliate, consultant or agent to the extent necessary for the performance of this Agreement provided such disclosure is subject to obligations equivalent to those set out in this Agreement. Each party shall use its best endeavours to procure that any such employee, consultant or agent complies with such obligations. Each party will be responsible to the other party in respect of any disclosure or use of such Confidential Information by a person to whom disclosure is made.

24.3 The obligations of confidentiality in this Clause 24 do not extend to any Confidential Information that the party that wishes to disclose or use can show:

(a) is or becomes generally available to the public other than as a result of a breach of the obligations of confidentiality under this Agreement; or

(b) was in its written records prior to the date of this Agreement and not subject to any confidentiality obligations; or

(c) was or is disclosed to it by a third party entitled to do so; or

(d) the parties agree in writing is not Confidential Information or may be disclosed; or

(e) is required to be disclosed under any Applicable Law, or by order of a court or governmental body or authority of competent jurisdiction.

24.4 Press Releases. UGNX and Kyowa Kirin shall consult in advance and reasonably cooperate in the method and manner of any press release regarding this Agreement and any activity related thereto. For clarity, following any press release issued pursuant to this Clause 24.4, UGNX and Kyowa Kirin may each disclose to third parties the information set forth in such

press release without the need for further approval by the other. Notwithstanding the foregoing, each party may make filings to the U.S. Securities and Exchange Commission (SEC) or similar requirements under Applicable Law, provided, that such party shall ensure that any such release will be limited in its disclosure only to information that is required for such disclosing party to be in compliance with Applicable Law.

25 PARTIES

25.1 This Agreement may not be assigned by either of the parties without the prior written consent of the other party; provided, however, either party may assign this Agreement in its entirety without such consent to any of its Affiliates, to any purchaser of all, or substantially all, of its assets or to any successor corporation resulting from any merger, consolidation, share exchange, or other similar transaction, and provided further that either party may assign or sell its rights to receive any amounts due hereunder.

25.2 A person who is not a party to this Agreement has no rights to enforce any provision of this Agreement.

25.3 The rights of the parties to terminate, rescind or agree any variation, waiver or settlement under this Agreement are not subject to the consent of any person that is not a party to this Agreement.

25.4 Neither party may pledge the credit of the other party nor represent itself as being the other party nor an agent, partner, employee or representative of the other party and neither party may hold itself out as such nor as having any power or authority to incur any obligation of any nature, express or implied, on behalf of the other. Nothing in this Agreement, and no action taken by the parties pursuant to this Agreement creates, or is deemed to create, a partnership or joint venture or relationship of employer and employee or principal and agent between the parties.

26 CONSTRUCTION AND INTERPRETATION OF THIS AGREEMENT

26.1 Entire Agreement

(a) This Agreement contains the entire agreement between the parties in relation to its subject matter and supersedes any prior arrangement, understanding written or oral agreements between the parties in relation to such subject matter.

(b) The parties acknowledge that this Agreement has not been entered into wholly or partly in reliance on, nor has either party been given, any warranty, statement, promise or representation by the other or on its behalf other than as expressly set out in this Agreement.

(c) All warranties and conditions, terms and conditions not set out in this Agreement whether implied by statute or otherwise are excluded to the extent permitted by law.

(d) Nothing in this Clause 26 will exclude any liability in respect of misrepresentations made fraudulently.

26.2 Precedence

(a) In the event of a conflict or ambiguity the order of precedence for this Agreement and the documents attached to or referred to in this Agreement are as follows:

(i) first the Clauses of this Agreement; and

(ii) then second the Schedules to this Agreement.

(iii) then the Quality Agreement

(b) Notwithstanding the foregoing, in the event of a conflict or ambiguity between any term of this Agreement (including anything contained within its Schedules) and the Quality Agreement or pharmacovigilance agreement concerning the Product, the term provided in the Quality Agreement or pharmacovigilance agreement shall take precedence in as far as the conflict or ambiguity concerns a quality or pharmacovigilance matter respectively.

26.3 Severability of Provisions

If at any time any part of this Agreement is held to be or becomes void or otherwise unenforceable for any reason under any applicable law, the same shall be deemed omitted from this Agreement and the validity and/or enforceability of the remaining provisions of this Agreement shall not in any way be affected or impaired as a result of that omission.

26.4 Waiver

The rights and remedies of either party in respect of this Agreement shall not be diminished, waived or extinguished by the granting of any indulgence, forbearance or extension of time granted by that party to the other nor by any failure of, or delay in ascertaining or exercising any such rights or remedies. Any waiver of any breach of this Agreement shall be in writing. The waiver by either party of any breach of this Agreement shall not prevent the subsequent enforcement of that provision and shall not be deemed to be a waiver of any subsequent breach of that or any other provision.

27 CONTRACT ADMINISTRATION

27.1 Variation

No purported alteration or variation of this Agreement shall be effective unless it is in writing, refers specifically to this Agreement and is signed by a director of each of the parties to this Agreement.

27.2 Language

This Agreement is entered into in the English language. All amendments or correspondence concerning or relating to this Agreement and all notices given and all documentation to be delivered by either party to the other under this Agreement shall be in writing in the English language or shall be accompanied by an English translation prepared by such person or body as the parties shall have approved in advance. If there is any conflict in meaning between the English language version and any version or translation of this Agreement in any other language the English version shall prevail.

27.3 Counterpart Signatures

This Agreement may be executed in any number of counterparts, each of which when executed shall constitute an original of this Agreement, but all the counterparts together constitute the same Agreement. No counterpart shall be effective until each party has executed at least one counterpart.

27.4 Further Actions Required

Each of the parties shall, and shall use their reasonable endeavours to procure that any necessary third parties shall, execute and deliver to the other party such other instruments and documents and take such other action as may reasonably be required for the purpose of giving full effect to this Agreement.

27.5 Notices

(a) Any notices sent under this Agreement must be in writing.

(b) Notices may be served in the ways set out below at the addresses set out at the top of this Agreement or at such other address as the relevant party may give notice to the other party for the purpose of service of notices under this Agreement and, the following table sets out the respective deemed time and proof of service:

Manner of Delivery	**Deemed time of delivery**	**Proof of Service**
Personal delivery/Cour	On delivery provided delivery between 9.00am and 5.00pm on Business Day	properly addressed and delivered
Prepaid international mail postal service	9.00am on the fifth Business D after posting	properly addressed prepaid a posted

(c) For the purpose of Clause 27.5(b) and calculating deemed receipt all references to time are local time in the place of deemed receipt.

28 DISPUTE RESOLUTION PROCEDURE

28.1 Disputes. The parties recognize that disagreements as to certain matters may from time to time arise out of this Agreement. The parties agree that such disagreements are to be governed in accordance with this Clause 28. Disagreements that are claims, counterclaims, demands, causes of action, disputes or controversies both arising out of this Agreement and related to the performance, enforcement, breach or termination of this Agreement are each, a "**Dispute**". For the avoidance of doubt, Dispute does not include any claims, counterclaims, demands, causes of action, disputes or controversies regarding a party's use of any Intellectual Property Rights of the other party, where such use is not expressly granted by the other party.

28.2 In the event of any Dispute under this Agreement, the parties shall refer such dispute to [***] for attempted resolution by good faith negotiations within [***] days after such referral is made.

28.3 Agreement to Arbitrate. If the parties fail to resolve any Dispute pursuant to Clause 28.2, either party may submit that Dispute for final resolution by binding arbitration administered by the International Chamber of Commerce ("**ICC**") in accordance with its Rules of Arbitration (the "**Rules**") then in force, to the extent such Rules are not inconsistent with the provisions of this Agreement.

28.4 Number and Appointment of Arbitrators. Except as provided by this Clause 28.4 or in Clause 28.5, the appointment and confirmation of the arbitrators shall be made in accordance with the relevant provisions of the Rules. The arbitral tribunal shall be composed of three (3) arbitrators (the "**Tribunal**") to be appointed in accordance with the Rules, except as expressly provided for herein. Each party shall select one (1) arbitrator from the list of available ICC arbitrators and such arbitrators shall jointly appoint the third arbitrator who shall act as the chairman of the Tribunal (the "**Chairman**"). In the event any arbitrator becomes unable to serve, that arbitrator will be replaced in the same manner in which he or she was appointed. If either party fails to appoint an arbitrator within [***] days of the initiation of arbitration, the other party may request the ICC to appoint such co-arbitrator (for the non-responsive party). Such appointment shall be binding on the parties. If the arbitrators selected by the parties cannot agree on a Chairman within [***] days after they have been selected, then the ICC shall appoint the Chairman upon request by either party.

28.5 Confidentiality. Except to the extent necessary for proceedings relating to enforcement of the arbitration agreement, the award, or other related rights of the parties, the fact of the arbitration, the arbitration proceeding itself, all evidence, written statements or other documents exchanged or used in the arbitration and the Tribunal's award will be maintained in confidence by the parties to the fullest extent permitted by law. However, a violation of this covenant will not affect the enforceability of this agreement to arbitrate or of the Tribunal's award.

28.6 Costs. Each party shall [***]. The Tribunal may also fix such costs and expenses proportionate to the extent each party prevails in the arbitration, as the circumstances may warrant. If a party fails to proceed with arbitration, unsuccessfully challenges the arbitration award or fails to comply with the arbitration award, the other party will be entitled to costs, including reasonable

attorneys' fees and disbursements, for having to compel arbitration or defend or enforce the award.

28.7 Notwithstanding the provisions of this Clause 28, either party may (unless agreed otherwise in writing) take proceedings or seek remedies before the courts or any competent authority of any country for injunctive relief or interlocutory remedies in relation to any breach of this Agreement or infringement by the other party of that party's Intellectual Property Rights, confidentiality rights or other such rights that without which would otherwise result in substantial financial or commercial harm.

29 LAW AND JURISDICTION

29.1 Resolution of all disputes arising out of or related to this Agreement or the performance, enforcement, breach or termination of this Agreement and any remedies relating thereto, will be governed by and construed under the substantive laws of the State of New York, U.S.A., without reference to any choice of law principles thereof that would cause the application of the laws of a different jurisdiction.

IN WITNESS OF THE ABOVE the parties have signed this Agreement on the date written at the head of this Agreement.

SIGNED for and on behalf of **KYOWA KIRIN**
/s/ Tara D'Orsi
Name: Tara D'Orsi
Title: General Counsel KYOWA KIRIN, INC.

SIGNED for and on behalf of **UGNX** by

/s/ Siegfried Hackl

Name: Siegfried Hackl Title: SVP Product Supply
ULTRAGENYX PHARMACEUTICAL INC.

SCHEDULE 1

Price and Payment

1. MINIMUM SUPPLY PRICE

Product	**Price**
KRN23 in all commercialized formulations, including, but not limited to 10mg, 20mg and 30mg presentations, in fully-finished form	USD$[***] per vial

2. PAYMENT AND ROYALTIES

(a) Within [***] days of delivery of Product to UGNX by Kyowa Kirin, Kyowa Kirin will invoice and UGNX shall pay an amount equal to the Minimum Supply Price multiplied by the number of naked vials of Product delivered (the "**Total Minimum Supply Price**").

(b) In the event that the Total Minimum Supply Price in the relevant [***] is less than the Agreed Supply Price, UGNX shall [***] within [***] days of the end of [***].

(c) In the event that the Total Minimum Supply Price is greater than the Agreed Supply Price, Kyowa Kirin shall [***] within [***] days of the end of [***].

3. NET SALES

3.1 "**Net Sales**" means, with respect to the Product, the gross amounts invoiced by UGNX or its Affiliates ("**Selling Party**") to any third party for sales of the Product in the Territory (for the avoidance of doubt, to include any revenue received in relation to supply of the Product in the Territory, whether or not strictly deemed a sale), less the following items, provided that they are bona fide:

(a) actual credits, refunds or allowances to third party customers for spoiled, damaged, rejected, recalled, outdated and reasonably returned Product;

(b) discounts, including cash, volume, quantity and other trade discounts, charge- back payments, and rebates and allowances actually granted, incurred or allowed in the ordinary course of business, as well as government-required discounts and allowances (including government rebates and other price reductions), and other reductions, concessions and allowances that effectively reduce the selling price to the Selling Party;

(c) transportation charges, freight, postage and insurance (but only insurance related to protecting the particular shipment against physical loss or damage); and

(d) sales, use or excise taxes and import/export duties or tariffs and similar governmental charges actually due or incurred in connection with the sales of such Product.

3.2 Components of Net Sales shall be determined in the ordinary course of business in accordance with GAAP (as applicable in the country of sale), consistently applied.

3.3 Net Sales shall include, for the Product, [***].

3.4 For the purposes of determining when a sale of any Product occurs for purposes of calculating Net Sales, the sale will be [***]. For purposes of this Agreement, “Accounting Standards” means U.S. generally accepted accounting principles as consistently applied throughout the applicable periods indicated herein by or on behalf of the relevant Selling Party.

3.5 For the purposes of determining Net Sales, a "sale" shall not include transfers or dispositions, at no cost or below cost, of the Product for charitable, compassionate, non-clinical, clinical or regulatory purposes or for promotional samples or free goods.

3.6 Amounts invoiced by the Selling Party for the sale of Product to another Affiliate for resale to a third party shall not be included in the computation of Net Sales hereunder.

3.7 In the event that the Selling Party sells the Product:

(a) to a third party in a bona fide arm's length transaction, for material consideration, in whole or in part, other than cash (but excluding, for the avoidance of doubt, consideration in the form of non-financial legal terms and conditions incident to sale including, for clarity, the supply of Product for non- commercial purposes substantially at cost);

(b) to a third party in other than a bona fide arm's length transaction; or

(c) with discounts of Product that are disproportional to the discounts of other products sold by the Selling Party in conjunction with such Product,

then the Net Sales price for such Product shall be deemed to be the standard invoice price then being invoiced by the Selling Party in an arm's length transaction with similar customers in the Territory, less typical deductions as accounted for in 3.1(a)(c) and (d).

3.8 In the event that the Selling Party includes one or more Product as part of a bundle of products, the price for such Product shall be deemed to be the standard invoice price for such Product when sold separately and not as part of a bundle of products. In the event that no separate prices are charged in the applicable transaction, then Net Sales for such bundle shall be determined based on the list price for the Product and the other products or services in the relevant county during the accounting period in which the sale was made. If no list price exists in such country for the Product or the other products or services that are part of the bundle, then Net Sales for such bundle shall

be equitably determined based on the fair market value of the Product relative to that of the other products or services.

3.9 Any dispute between the parties with respect to the determination of such market value shall be finally resolved pursuant to Clause 28 of the Agreement.

4. RECORDS AND AUDIT RIGHT

4.1 UGNX will maintain complete and accurate records in sufficient detail to permit Kyowa Kirin to confirm the accuracy of the calculation of payments under this Agreement. Upon reasonable prior notice, such records shall be available during regular business hours for a period of [***] from the end of the calendar year to which they pertain for examination at the expense of Kyowa Kirin, and not more often than [***] each [***], for the sole purpose of verifying the amounts payable hereunder (e.g. the calculation of the Total Minimum Supply Price and Net Sales) and may include the use of an independent certified public accountant selected by Kyowa Kirin and reasonably acceptable to UGNX. Any such auditor shall not disclose UGNX's Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by UGNX or the amount of payments due under this Agreement during the prior [***]. Any amounts shown to be owed but unpaid shall be paid within [***] from the accountant's report, [***] (as set forth in Clause 10.5 of the Agreement) from the original due date, unless challenged as provided below. Any amounts shown to have been overcharged or overpaid shall be refunded within [***] from the accountant's report. [***].

4.2 If UGNX challenges the results of the audit in good faith, UGNX shall be entitled [***] to obtain a second independent certified public accountant to confirm the accuracy of the first audit. If the results of the confirmatory audit are substantially similar to the results of the first audit, any amounts owed by UGNX shall be paid in accordance with the procedures above. If the results of the confirmatory audit are not substantially similar to the results of the first audit, each party shall cause its respective auditors to identify the discrepancy and to agree on a final amount owed (as the case may be) by UGNX that shall be final and binding on the parties. If the auditors cannot resolve the discrepancy, the parties shall mutually agree on a third independent certified public accountant to audit the discrepancy and provide a final amount owed (as the case may be) by UGNX, which shall be binding on the parties. The costs of such third audit shall be [***]. Amounts owed or overpaid as determined by such final audit shall be paid or refunded in accordance with the procedures above

5. [***] REPORTING

5.1 UGNX shall provide Kyowa Kirin with a [***] Report within [***] days of the end of each [***].

5.2 "**[***] Report**" means a report which sets out, as a minimum, the following information:

(a) Unit sales of the Product in the Territory during the previous [***]; and

(b) Net Sales of the Product in the Territory during the previous [***].

6. EXCHANGE RATE

6.1 The rate of exchange to be used in computing the amount of currency equivalent in US Dollars owed to a party for royalties and Agreed Supply Price under this Agreement shall be equal to the average exchange rate, over the applicable Quarter, between each currency of origin and USD as reported by [***] or an equivalent resource as agreed by the parties, on the last Business Day of the [***] in which the applicable Net Sales were made.

Exhibit 10.16

[***] = 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.

AMENDMENT NO.1 TO SUPPLY AGREEMENT

This Amendment No.1 to the Supply Agreement ("Amendment No.1"), effective as of September 13, 2024 ("Effective Date"), is made and entered into by and between Kyowa Kirin, Inc., a corporation organized and existing under the laws of Delaware, having its principal place of business at 510 Carnegie Center, Princeton, NJ 08540 ("Kyowa Kirin") and Ultragenyx Pharmaceutical Inc., a company organized and existing under the laws of Delaware, having its principal place of business at 60 Leveroni Court, Novato, CA 94949 ("UGNX"). UGNX and Kyowa Kirin may be referred to herein individually as a "Party" or collectively as the "Parties."

WHEREAS, UGNX and Kyowa Kirin entered into that certain Supply Agreement made as of October 27, 2020 ("Agreement").

WHEREAS, the Parties wish to hereby amend the Agreement as set forth below.

NOW, THEREFORE, in consideration of the promises, the mutual covenants contained herein and other valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree to amend the Agreement as follows:

1. Section 1.1 in the Agreement is hereby amended to include the following definition:

"Warehouse A Product handling and/or storage location directly managed by Kyowa Kirin or indirectly managed through Kyowa Kirin's approved supplier network, whereby Kyowa Kirin's approved supplier having previously satisfied the requirements of Kyowa Kirin's supplier audit criteria and supported by an appropriate quality technical agreement;"

2. Section 6.1 in the Agreement is hereby deleted in its entirety and replaced with the following:

"6.1 During the Term of this Agreement, Kyowa Kirin shall supply Product as naked, unlabelled product. Product will be supplied to UGNX from the bulk drug Product supply maintained or made available at Kyowa Kirin's Warehouse (as defined herein) or Kyowa Kirin's approved third-party packaging facility(ies) as outlined in Section 7.2. Kyowa Kirin agrees to maintain an inventory of sufficient Product as mutually agreed through the joint sales and operations planning process."

3. Section 7.2 in the Agreement is hereby deleted in its entirety and replaced with the following:

"7.2 Product will be shipped by Kyowa Kirin [***] to a regional packaging facility located in [***] or to a Kyowa Kirin qualified Warehouse in the United States, or to the Kyowa Kirin regional packaging facility located in [***], or to any other such Kyowa Kirin packaging facility as approved in advance by UGNX. Kyowa Kirin will coordinate the shipment of the Product into the United States and the Product receipt at Kyowa Kirin's qualified Warehouse or packaging facility. Products shall be made available to UGNX from Kyowa Kirin approved inventory, having already

been transported from the point of manufacture using Kyowa Kirin qualified shipping lanes.”

4. Section 7.3 in the Agreement is hereby deleted in its entirety and replaced with the following:

> "7.3 All Product supplied by Kyowa Kirin that is (i) shipped from the regional packaging facility located at [***] shall be examined and checked upon transfer or delivery to UGNX (or its designee at the regional packaging site) and (ii) shipped from a qualified Kyowa Kirin Warehouse, shall be examined and checked upon transfer or delivery to UGNX's packaging facility at [***] in order to ascertain that the Product complies with the lot release information, quantity, and Inventory Acceptance Requirements."

5. Section 8.1 in the Agreement is hereby deleted in its entirety and replaced with the following:

> "8.1 Title and risk of loss to Products shall pass to UGNX upon transfer or delivery to UGNX or its designee at: (i) the regional packaging facility located in [***] for the Products shipped to such facility, or (ii) at Kyowa Kirin's Warehouse for the Products shipped to Kyowa Kirin's Warehouse for further shipment by UGNX to UGNX packaging facility at [***] ."

6. Except as expressly provided in this Amendment No.1, all other terms, conditions and provisions of the Agreement shall continue in full force and effect as provided therein. Capitalized terms used in this Amendment No.1 that are not otherwise defined herein, shall have the meanings assigned to them in the Agreement.

7. This Amendment No. 1 shall inure to the benefit of, and be binding upon, the Parties hereto and their respective heirs, successors, trustees, transferees and assigns.

8. This Amendment No.1 may be executed in two or more counterparts, each of which shall be deemed an original and all of which shall constitute together the same instrument. The Parties to this Amendment No.1 agree that a copy of the original signature (including an electronic copy) may be used for any and all purposes for which the original signature may have been used. The Parties agree they will have no rights to challenge the use or authenticity of this document based solely on the absence of an original signature.

[Signature page follow on next page]

IN WITNESS WHEREOF, the Parties have duly authorized persons executed this Amendment No.1 as of the Effective Date.

ULTRAGENYX PHARMACEUTICAL INC.	KYOWA KIRIN, INC.
By: /s/ Siegfried Hackl	By: /s/ Paul Jesta
Siegfried Hackl	Paul Jesta
Printed Name	Printed Name
SVP Product Supply	EVP - Operations
Title	Title
13-Sep-2024	19-Sep-2024
Date	Date

Exhibit 10.38

[***] = 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.

Name: [●]
Target Number of Performance Stock Units subject to Award: [●]
Date of Grant: [●]

ULTRAGENYX PHARMACEUTICAL INC.
2023 INCENTIVE PLAN

PERFORMANCE STOCK UNIT AGREEMENT (2024)

This agreement (this "Agreement") evidences an award (the "Award") of performance stock units (the "Performance Stock Units") granted by Ultragenyx Pharmaceutical Inc. (the "Company") to the undersigned (the "Grantee") pursuant to and subject to the terms of the Ultragenyx Pharmaceutical Inc. 2023 Incentive Plan (as amended from time to time, the "Plan"), which is incorporated herein by reference.

1.Grant of Performance Stock Units. The Company grants to the Grantee on the date set forth above (the "Date of Grant") an award consisting of the right to receive on the terms provided herein and in the Plan, one share of Stock with respect to each Performance Stock Unit forming part of the Award, in each case, subject to adjustment pursuant to Section 7(b) of the Plan in respect of transactions occurring after the date hereof.

2.Meaning of Certain Terms. Except as otherwise defined herein, all capitalized terms used herein have the same meaning as in the Plan.

3.Vesting.

(a)Unless earlier terminated, forfeited, relinquished or expired, and subject to the Grantee's continued employment through the applicable vesting dates, (i) 1/3 (or 33.4%) of the Performance Stock Units shall vest in accordance with Section 3(b) (the "Revenue PSUs"), (ii) 1/3 (or 33.3%) of the Performance Stock Units shall vest in accordance with Section 3(c) (the "TSR PSUs") and (iii) 1/3 (or 33.3%) of the Performance Stock Units shall vest in accordance with Section 3(d) (the "Strategic PSUs").

(b)The Revenue PSUs shall vest as follows:

(i) If the Administrator certifies that the revenue performance metric set forth in Appendix A attached hereto (the "Revenue Vesting Metric") has been achieved at at least the threshold level of performance during the period beginning on January 1, 2024 and ending on December 31, 2025 (the "Revenue Performance Period"), 100% of the Earned Revenue PSUs (as determined pursuant to Appendix A) shall vest on the later of (x) the date on which the Administrator certified such achievement and (y) March 1, 2026.

Notwithstanding anything to the contrary in this Section 3(b), in the event that the Company fails to achieve the threshold level of performance under the Revenue Vesting Metric during the Revenue Performance Period, the

vesting of the Revenue PSUs shall immediately cease and all of the Revenue PSUs shall be immediately forfeited as of the last day of the Revenue Performance Period.

(c)If the Administrator certifies that the relative total stockholder return performance metric set forth in Appendix B attached hereto (the "TSR Vesting Metric") has been achieved at at least the threshold level of performance during the period beginning on January 1, 2024 and ending on December 31, 2026 (the "TSR and Strategic Performance Period"), 100% of the Earned TSR PSUs (as determined pursuant to Appendix B) shall vest on the later of (x) the date on which the Administrator certified such achievement and (y) March 1, 2027.

(d)If the Administrator certifies that the strategic performance metric set forth in Appendix C attached hereto (the "Strategic Vesting Metric") has been achieved by at least the threshold level of performance during the TSR and Strategic Performance Period, 100% of the Earned Revenue PSUs (as determined pursuant to Appendix C) shall vest on the later of (x) the date on which the Administrator certified such achievement and (y) March 1, 2027.

Notwithstanding anything to the contrary in this Section 3(d), in the event that the Company fails to achieve the threshold level of performance under the Strategic Vesting Metric during the TSR and Strategic Performance Period, the vesting of the Strategic PSUs shall immediately cease and all of the Strategic PSUs shall be immediately forfeited as of the last day of the TSR and Strategic Performance Period.

(e)Notwithstanding anything to the contrary in Section 3(b), Section 3(c) and Section 3(d) above and subject to the conditions set forth below, if the Company consummates a Covered Transaction prior to the end of the Revenue Performance Period and/or TSR and Strategic Performance Period, the Performance Stock Units granted hereby that have not otherwise vested or been terminated, forfeited, relinquished or expired prior to the Covered Transaction shall automatically become a number of time-vested restricted stock units ("Restricted Stock Units") assuming the greater of (i) the target level of performance or (ii) (x) with respect to the Revenue Vesting Metric and the Strategic Vesting Metric, the expected (as determined by the Administrator) level of performance and (y) with respect to the TSR Vesting Metric, the actual level of performance through the date of the Covered Transaction, which Restricted Stock Units shall vest on the first anniversary of the Covered Transaction, subject to Grantee's continued employment through that date. If the Administrator certifies that the Revenue Vesting Metric and/or the Strategic Vesting Metric has been achieved during the Revenue Performance Period and TSR and Stratetic Performance Period, as applicable, and prior to the Covered Transaction, the applicable time-based vesting dates for those Earned Performance Stock Units shall not be affected by any Covered Transaction, and such Earned Performance Stock Units shall continue to vest based on their applicable time-based vesting dates.

4.Delivery of Stock. The Company shall deliver to the Grantee as soon as practicable upon the vesting of the Performance Stock Units (or, if applicable, Restricted Stock Units) or any portion thereof, but in all events no later than March 15th of the year following the year in which such units vest, one share of Stock with respect to each such vested unit, subject to the terms of the Plan and this Agreement.

5.Dividends; Other Rights. The Award shall not be interpreted to bestow upon the Grantee any equity interest or ownership in the Company or any Affiliate prior to the date on which the Company delivers shares of Stock to the Grantee (if any). The Grantee is not entitled to vote any shares of Stock by reason of the granting of this Award or to receive or be credited with any dividends declared and payable on any share of Stock prior to the date on which any such share is delivered to the Grantee hereunder. The Grantee shall have the rights of a shareholder only as to those shares of Stock, if any, that are actually delivered under this Award.

6.Forfeiture; Recovery of Compensation.

(a)The Administrator may cancel, rescind, withhold or otherwise limit or restrict the Award at any time if the Grantee is not in compliance with all applicable provisions of this Agreement and the Plan.

(b)By accepting the Award the Grantee expressly acknowledges and agrees that his or her rights, and those of any permitted transferee of the Award, under the Award to any Stock acquired under the Award or proceeds from the disposition thereof, are subject to (i) Section 6(a)(5) of the Plan (including any successor provision) and (ii) recoupment in accordance with any clawback policy adopted by the Company, as may be modified from time to time by the Company in its discretion. Nothing in the preceding sentence shall be construed as limiting the general application of Section 10 hereof. No recovery of compensation under a clawback policy or under Section 6(a)(5) of the Plan will be an event giving rise to a right to resign for "good reason" or "constructive termination" (or similar term) under any agreement with the Company

7.Nontransferability. Neither the Award nor the Performance Stock Units (or, if applicable, Restricted Stock Units) may be transferred except as expressly permitted under Section 6(a)(3) of the Plan.

8.Certain Tax Matters.

(a)The Grantee expressly acknowledges and agrees that the Grantee's rights hereunder, including the right to be issued shares of Stock upon the vesting of the Performance Stock Units (or, if applicable, Restricted Stock Units) (or any portion thereof), are subject to the Grantee's promptly paying, or in respect of any later requirement of withholding being liable promptly to pay at such time as such withholdings are due, to the Company in cash (or by such other means as may be acceptable to the Administrator in its discretion) all taxes required to be withheld, if any (the "Tax Withholding Obligation"). No shares of Stock will be transferred pursuant to the vesting of the Performance Stock Units (or, if applicable, Restricted Stock Units) (or any portion thereof) unless and until the Grantee or the person then holding the Award has remitted to the Company an amount in cash sufficient to satisfy any federal, state, or local withholding tax requirements then due and has committed (and by accepting this Award the Grantee shall be deemed to have committed) to pay in cash all tax withholdings required at any later time in respect of the transfer of such shares, or has made other arrangements satisfactory to the Company with respect to such taxes. The Grantee also authorizes the Company and its subsidiaries to withhold such amount from any amounts otherwise owed to the Grantee, but nothing in this sentence shall be construed as relieving the Grantee of any liability for satisfying his or her obligations under the preceding provisions of this Section 8.

(b)The Grantee expressly acknowledges that the Grantee's acceptance of this Agreement constitutes the Grantee's instruction and authorization to the Company and any brokerage firm determined acceptable to the Company for such purpose to sell on the Grantee's behalf a whole number of shares from those shares of Stock issuable to the Grantee as the Company determines to be appropriate to generate cash proceeds sufficient to satisfy the applicable Tax Withholding Obligation, and to transfer the proceeds from the sale of such Stock from the Grantee's securities account established with the brokerage service provider for the settlement of the Grantee's vested Performance Stock Units (or, if applicable, Restricted Stock Units) to any account held in the name of the Company. Such shares will be sold on the date of vesting or as soon thereafter as practicable. Grantee will be responsible for all brokers' fees and other costs of sale, which fees and costs may be deducted from the proceeds of the foregoing sale of Stock, and Grantee agrees to indemnify and hold the Company and any brokerage firm selling such Stock harmless from any losses, costs, damages, or expenses relating to any such sale. To the extent the proceeds of such sale exceed Grantee's Tax Withholding Obligation, such excess cash will be deposited into the securities account established with the brokerage service provider for the settlement of Grantee's vested Performance Stock Units (or, if applicable, Restricted Stock Units). Grantee acknowledges that the Company or its designee is under no obligation to arrange for such sale at any particular price, and that the proceeds of any such sale may not be sufficient to satisfy Grantee's Tax Withholding Obligation. Accordingly, Grantee agrees to pay to the Company as soon as practicable, including through additional payroll withholding, any amount of the Tax Withholding Obligation that is not satisfied by the sale of shares described above. Unless otherwise authorized by the Administrator in its sole discretion, the sale of Stock will be the primary method used by the Company to satisfy the applicable Tax Withholding Obligation.

(c)The Grantee expressly acknowledges that because this Award consists of an unfunded and unsecured promise by the Company to deliver Stock in the future, subject to the terms hereof, it is not possible to make a so-called “83(b) election” with respect to the Award.

9.Effect on Employment. Neither the grant of the Award, nor the issuance of Shares upon vesting of the Award, will give the Grantee any right to be retained in the employ or service of the Company or any of its Affiliates, affect the right of the Company or any of its Affiliates to discharge or discipline such Grantee at any time, or affect any right of such Grantee to terminate his or her Employment at any time.

10.Provisions of the Plan. This Agreement is subject in its entirety to the provisions of the Plan, which are incorporated herein by reference. A copy of the Plan as in effect on the Date of Grant has been furnished to the Grantee. By accepting the Award, the Grantee agrees to be bound by the terms of the Plan and this Agreement. In the event of any conflict between the terms of this Agreement and the Plan, the terms of the Plan shall control.

11.Acknowledgments. The Grantee acknowledges and agrees that (a) this Agreement may be executed in two or more counterparts, each of which shall be an original and all of which together shall constitute one and the same instrument, (b) this agreement may be executed and exchanged using facsimile, portable document format (PDF) or electronic signature, which, in each case, shall constitute an original signature for all purposes hereunder and (c) such signature by the Company will be binding against the Company and will create a legally binding agreement when this Agreement is countersigned by the Grantee.

[The remainder of this page is intentionally left blank.]

IN WITNESS WHEREOF, the Company has caused this Agreement to be executed by its duly authorized officer.

ULTRAGENYX PHARMACEUTICAL INC.

By:
Name:
Title:

Dated:

Acknowledged and Agreed:

By:
[Grantee's Name]

DOCPROPERTY "DOCID" * MERGEFORMAT

APPENDIX A

The performance metric applicable to the Revenue PSUs shall be GAAP revenue for the Company over the Revenue Performance Period, with the number of Earned Revenue PSUs equal to the number of Revenue PSUs subject to the Award multipled by the applicable percentage set forth in the following table:

Level of Performance	Aggregate GAAP Revenue[(1)] for FY 2024 and FY 2025	Earned Revenue PSUs[(2)]
Threshold	$[***]	50%
Target	$[***]	100%
Maximum	$[***]	200%

(1) Company required to achieve the threshold target [***].

(2) For performance between threshold and target and between target and maximum, the percentage of the Revenue PSUs that become Earned Revenue PSUs will be determined on a straight-line interpolated basis.

APPENDIX B

The performance metric applicable to the TSR PSUs shall be the Company's Total Stockholder Return (as defined below) relative to the Total Stockholder Return of the companies in the NASDAQ Biotechnology Index (NBI) (the "Peer Group"), with the number of Earned TSR PSUs equal to the number of TSR PSUs subject to the Award multiplied by the applicable percentage set forth in the following table:

Level of Performance	TSR Percentile[(1)]	Earned TSR PSUs[(2)]
Threshold	25th	25%
Target	50th	100%
Stretch	75th	150%
Maximum	90th	200%

(1) TSR Percentile is calculated based on the Company's ranking within the Peer Group based on its Total Stockholder Return as compared to the Total Stockholder Return of each member of the Peer Group.

(2) For performance between threshold and target, between target and stretch and between stretch and maximum, the percentage of the TSR PSUs that become Earned TSR PSUs will be determined on a straight-line interpolated basis.

"Total Stockholder Return" of the Company and of each member of the Peer Group shall be determined pursuant to the following formula:

$$\text{Total Stockholder Return} = \frac{(\text{Final Stock Price} - \text{Initial Stock Price}) + \text{Reinvested Dividends}}{\text{Initial Stock Price}}$$

For purposes of this formula, (a) "Final Stock Price" shall be the relevant company's average closing stock price for the two-month period preceding the last trading day of the TSR Performance Period, (b) "Initial Stock Price" shall be the relevant company's average closing stock price for the two-month period preceding the first trading day of the Performance Period, and (c) "Reinvested Dividends" shall be the aggregate number of shares (including fractional shares) that could have been purchased during the TSR Performance Period had each cash dividend paid on a single share during that period been immediately reinvested in additional shares (or fractional shares) at the closing stock price on the applicable dividend payment date. Each of the foregoing amounts shall be equitably adjusted for stock splits, stock dividends, recapitalizations and other similar events affecting the shares in question without the issuer's receipt of consideration.

APPENDIX C

The performance metric applicable to the Strategic PSUs shall be based on the number of strategic goals (as listed below) achieved over the TSR and Strategic Performance Period, with the number of Earned Strategic PSUs equal to the number of Strategic PSUs subject to the Award multipled by the applicable percentage set forth in the following table:

Strategic Goals

1. [***]
2. [***]
3. [***]
4. [***]
5. [***]

Level of Performance	Number of Strategic Goals Achieved	Earned Revenue PSUs
Threshold	2 out of 5	50%
Target	3 out of 5	100%
Stretch	4 out of 5	150%
Maximum	5 out of 5	200%

Exhibit 10.77

Addendum #7 To The Lease Dated on or about July 1, 2011 By and Between Condiotti Enterprises, Inc. ("Lessor") And Ultragenyx Pharmaceutical Inc. ("Lessee")

On or about July 1, 2011 Lessor and Lessee entered into a lease and Addendum 1 for approximately 19,916 square feet, comprising the entire second floor of the Premises located at 60 Leveroni Court, Novato, California. Subsequent to the execution of that Lease, the parties have executed Addenda two through six (together, the "Lease"), which, in addition to such other terms and conditions agreed to facilitate operation of the Lease and the subject changes, have extended the term of the Lease to December 31, 2024 and expanded the space to include all of the Premises at 60 Leveroni Court (approximately 43,517 sf) and all of the Premises at 52 Leveroni Court (approximately 20,343 sf) and the first floor of the Premises located at 68 Leveroni Court (approximately 10,408 sf), bringing the total square footage subject to the Lease and Addenda to approximately 74,268 square feet.

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

112. The parties agree to extend the Term of the Lease to expire on December 31, 2026.

113. Upon execution of this Addendum #7, Tenant will vacate and surrender the Premises at 68 Leveroni Court and terminate its obligations under the Lease with respect to 68 Leveroni Court. Tenant shall ensure that upon execution of this Addendum, it will surrender of the Premises at 68 Leveroni Court to Landlord as required; specifically broom clean condition, removal of cabling, removal of telephone and internet wiring, removal of security equipment and wiring and removal of all personal property.

114. Tenant acknowledges and agrees that it accepts the retained Premises at 52 Leveroni Court and 60 Leveroni Court “AS-IS,” subject to the water leaks and HVAC units as notified by Tenant to Landlord in emails dated January 26, 2024, July 3, 2024, and July 31, 2024.

115. Base Monthly Rent for the remaining Premises at 52 and 60 Leveroni Court (approx. 63,860 sf) for the period January 1, 2025 through December 31, 2025 shall be at $102,176.00, and for the period of January 1, 2026 through December 31, 2026 shall be at $105,369.00.

116. Section 110 of Addendum 6 is hereby deleted.

117. Upon the expiration or early termination of the Lease, Tenant shall return the 52 and 60 Leveroni Court spaces in broom clean condition, with the removal of cabling, removal of telephone and internet wiring, removal of security equipment and wiring, and removal of personal property.

118. Once the space at 68 Leveroni Court has been vacated by the Tenant, Section 45 of Addendum 1 shall be amended to include a Letter of Credit in the amount of $105,369.00 which shall remain in effect until both spaces at 52 and 60 Leveroni Court have been vacated by the Tenant. All other provisions of Section 45 of Addendum 1 shall remain in full force and effect.

119. Each party to this Addendum #7 represents and agrees that commissions or fees of any kind incurred in relation to or as a result of this Addendum #7 shall be borne by the party incurring it.

120. Except as expressly modified by this Addendum #7 the Lease shall remain in full force and effect.

Agreed to this 22nd day of November, 2024.

Lessee

Approved and Executed By:

/s/ Emil Kakkis

Name: Title:

Emil Kakkis

Chief Executive Officer

Ultragenyx Pharmaceutical Inc.

Lessor

/s/ Jan Warz

Jan Warz, COO

Condiotti Enterprises, Inc.

Exhibit 10.84

FIFTH AMENDMENT TO LEASE AGREEMENT

THIS FIFTH AMENDMENT TO LEASE AGREEMENT (this "**Fifth Amendment**") is made as of this 25th day of November, 2024, between **ARE-MA REGION NO. 20, LLC**, a Delaware limited liability company ("**Landlord**"), and **ULTRAGENYX PHARMACEUTICAL INC.**, a Delaware corporation ("**Tenant**").

RECITALS:

A. Tenant and Landlord are parties to that certain Lease Agreement dated as of October 30, 2015, as amended by that certain First Amendment to Lease Agreement dated as of March 20, 2018, as further amended by that certain Second Amendment to Lease Agreement dated as of July 1, 2018, as further amended by that certain Third Amendment to Lease Agreement dated as of July 29, 2019 (the "**Third Amendment**"), and as further amended by that certain Amended and Restated Fourth Amendment to Lease Agreement dated as of August 4, 2020 (the "**Amended and Restated Fourth Amendment**") (as amended, the "**Lease**"). Pursuant to the Lease, Tenant leases from Landlord a total of approximately 40,060 rentable square feet of space consisting of (i) approximately 17,475 rentable square feet of laboratory/office space on the second floor of the Building, (ii) approximately 108 rentable square feet of storage space on the first floor of the Building, (iii) approximately 6,455 rentable square feet of laboratory/office space on the third floor of the Building, (iv) approximately 7,957 rentable square feet of laboratory/office space on the third floor of the Building commonly known as Suite 302, (v) approximately 130 rentable square feet of storage space on the first floor of the Building commonly known as Suite 100I,
(vi) approximately 7,805 rentable square feet of space on the third floor of the Building commonly known as Suite 306, and (vii) approximately 130 rentable square feet of storage space on the first floor of the Building commonly known as Suite 100H, (collectively, the "**Premises**") in that certain building located at 19 Presidential Way, Woburn, Massachusetts (the "**Building**"), as more particularly described in the Lease. Capitalized terms used herein without definition shall have the meanings defined for such terms in the Lease.

B. The term of the Lease is scheduled to expire on April 30, 2025.

C. Landlord and Tenant desire, subject to the terms and conditions set forth herein below, to amend the Lease to, among other things, extend the term of the Lease through April 30, 2028 (the "**Fifth Amendment Expiration Date**").

NOW, THEREFORE, in consideration of the mutual covenants herein expressed and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Tenant and Landlord agree as follows:

1. **Extension of Term**. The Term of the Lease is hereby extended through the Fifth Amendment Expiration Date. Tenant's occupancy of the Premises through the Fifth Amendment Expiration Date shall be on an "as-is" basis, and Landlord shall have no obligation to provide any tenant improvement allowance or to make any alterations to the Premises, except as set forth in Section 3.

2. **Base Rent**. Tenant shall continue to pay Base Rent as set forth in the Lease through April 30, 2025. Commencing on May 1, 2025, Tenant shall pay Base Rent in the amount of $55.00 per rentable square foot of the Premises per year. On May 1, 2026, and on each May 1st thereafter (each, an "**Adjustment Date**"), the Base Rent shall be increased by multiplying the Base Rent immediately before such Adjustment Date by 3% and adding the resulting amount to the Base Rent payable immediately before such Adjustment Date.

Notwithstanding anything to the contrary contained in this Section 2, so long as Tenant is not in default under the Lease (beyond all applicable notice and cure periods), Base Rent shall be abated during the period commencing on May 1, 2025, through August 31, 2025 (the "**Fifth Amendment Abatement Period**"). Tenant shall resume paying full Base Rent on the first day following the expiration of the Fifth

Amendment Abatement Period. For the avoidance of doubt, Tenant shall continue paying Operating Expenses and all other amounts payable under the Lease during the Fifth Amendment Abatement Period.

3. **Premises Improvements**. Landlord shall make available to Tenant a tenant improvement allowance in the amount of $5.00 per rentable square foot of the Premises (the "**Fifth Amendment Improvement Allowance**") for the design and construction of fixed and permanent improvements desired by and performed by Tenant and reasonably acceptable to Landlord in the Premises (the "**Premises Improvements**"), which Premises Improvements shall be constructed pursuant to a scope of work reasonably acceptable to Landlord and Tenant. The Fifth Amendment Improvement Allowance shall be available only for the design and construction of the Premises Improvements. The Fifth Amendment Improvement Allowance may not be used to purchase any furniture, personal property, data/cabling or other non-Building System materials or equipment. Tenant acknowledges that upon the expiration or earlier termination of the Term of the Lease, the Premises Improvements shall become the property of Landlord and may not be removed by Tenant. Tenant shall pay to Landlord administrative rent in the amount of 1% of the total costs of the Premises Improvements, which amount shall be payable out of the Fifth Amendment Improvement Allowance. Except for the Fifth Amendment Improvement Allowance, Tenant shall be solely responsible for all of the costs of the Premises Improvements. The Premises Improvements shall be treated as Alterations and shall be undertaken pursuant to Section 12 of the Lease. The contractor for the Premises Improvements shall be selected and engaged by Tenant, subject to Landlord's approval, which approval shall not be unreasonably withheld, conditioned or delayed. Prior to the commencement of the Premises Improvements, Tenant shall deliver to Landlord a copy of any contract with Tenant's contractors, and certificates of insurance from any contractor performing any part of the Premises Improvements evidencing industry standard commercial general liability, automotive liability, "builder's risk", and workers' compensation insurance. Tenant shall cause the general contractor to provide a certificate of insurance naming Landlord, Alexandria Real Estate Equities, Inc., and Landlord's lender (if any) as additional insureds for the general contractor's liability coverages required above.

During the course of design and construction of the Premises Improvements, Landlord shall reimburse Tenant for the cost of the Premises Improvements once a month against a draw request in Landlord's standard form, containing evidence of payment of the applicable costs and such certifications, lien waivers (including a conditional lien release for each progress payment and unconditional lien releases for the prior month's progress payments), inspection reports and other matters as Landlord customarily and reasonably obtains, to the extent of Landlord's approval thereof for payment, no later than 30 days following receipt of such draw request. Upon completion of the Premises Improvements (and prior to any final disbursement of the Fifth Amendment Improvement Allowance) Tenant shall deliver to Landlord the following items: (i) sworn statements setting forth the names of all contractors and subcontractors who did work on the Premises Improvements and final lien waivers from all such contractors and subcontractors; and (ii) "as built" plans, if available, for Premises Improvements. Notwithstanding the foregoing, if the cost of the Premises Improvements exceeds the Fifth Amendment Improvement Allowance, Tenant shall be required to pay such excess in full prior to Landlord having any obligation to fund any remaining portion of the Fifth Amendment Improvement Allowance. The Fifth Amendment Improvement Allowance shall only be available for use by Tenant for the construction of the Premises Improvements from the date of this Fifth Amendment through the date that is 12 months after the date of this Fifth Amendment (the "**Outside Fifth Amendment Improvement Allowance Date**"). Any portion of the Fifth Amendment Improvement Allowance which has not been properly requested by Tenant from Landlord on or before the Outside Fifth Amendment Improvement Allowance Date shall be forfeited and shall not be available for use by Tenant.

4. **Right to Extend Term**. Section 39(a) of the Lease is hereby deleted in its entirety and replaced with the following:

> (a) **Extension Rights**. Tenant shall have 1 right ("**Extension Right**") to extend the term of the Lease for 3 years (the "**Extension Term**") on the same terms and conditions as the Lease, as amended (other than with respect to Base Rent, the Work Letter and any TI Allowance) by giving Landlord written notice of its election to exercise the Extension Right at least 9 months prior, and no earlier than 12 months prior, to the expiration of the Fifth Amendment Expiration Date. Upon the commencement of the Extension Term, Base Rent

shall be payable at the Market Rate (as defined below). Base Rent shall thereafter be adjusted on each annual anniversary of the commencement of such Extension Term by a percentage as determined by Landlord and agreed to by Tenant at the time the Market Rate is determined. As used herein, "**Market Rate**" shall mean the rate that comparable landlords of comparable buildings have accepted in current transactions from non-equity (i.e., not being offered equity in the buildings) and nonaffiliated tenants of similar financial strength for space of comparable size, quality (including all Tenant Improvements, Alterations and other improvements) in laboratory/office buildings in the Route 128 N Marketplace submarket area for a comparable term, with the determination of the Market Rate to take into account all relevant factors, including tenant inducements, parking costs, leasing commissions, allowances or concessions, if any. Notwithstanding the foregoing, the Market Rate shall in no event be less than the Base Rent payable as of the date immediately preceding the commencement of such Extension Term.

If, on or before the date which is 180 days prior to the Fifth Amendment Expiration Date, Tenant has not agreed with Landlord's determination of the Market Rate and the rent escalations during the Extension Term after negotiating in good faith, Tenant shall be deemed to have elected arbitration as described in Section 4(b). Tenant acknowledges and agrees that, if Tenant has elected to exercise the Extension Right by delivering notice to Landlord as required in this Section 4(a), Tenant shall have no right thereafter to rescind or elect not to extend the term of the Lease for the Extension Term.

5. **Right to Expand**. For the avoidance of doubt, Tenant shall continue to have a right to expand the Premises pursuant to the terms of Section 8 of the Amended & Restated Fourth Amendment.

6. **Shared Space Arrangement.** The following new subsection (g) is added to Section 22 of the Lease:

"(g) **Shared Space Arrangement.** Notwithstanding anything to the contrary contained in the Lease, Tenant may from time to time enter into agreements (each, a "**Shared Space Arrangement**") with affiliates of Tenant (each, a "**Shared Space Occupant**"), pursuant to which such Shared Space Occupants may collectively occupy up to 15% of the Premises as "**Shared Space Area**" in the aggregate for a period not to exceed 12 months in the aggregate, and such Shared Space Arrangements shall not require Landlord's consent under Section 22; provided, however, that Tenant shall be required to provide Landlord with a copy of each such Shared Space Arrangement and, prior to the effective date of each such Shared Space Arrangement, Tenant and each Shared Space Occupant shall be required to execute an acknowledgment in the form of **Exhibit A** attached hereto. Tenant shall be fully responsible for the conduct of any Shared Space Occupant within the Shared Space Area and the Project, and Tenant's indemnification obligations set forth in the Lease shall apply with respect to the conduct of such parties within the Shared Space Area and Project. Tenant shall not be required to pay any Excess Rents with respect to any Shared Space Arrangements to Landlord. The rights with respect to a Shared Space Arrangement as provided for in this Section 6 is personal solely to Ultragenyx Pharmaceutical Inc. and may not be assigned or transferred to any other person or entity. Except as modified by this Section 22(g), all other terms of Section 22 shall remain in full force and effect."

7. **Lower Level Premises**. For the avoidance of doubt, the terms of the Third Amendment shall continue to apply with respect to the Lower Level Premises.

8. **OFAC**. Tenant and Landlord 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 Term of the Lease be listed on, the Specially Designated Nationals and Blocked Persons List, Foreign Sanctions Evaders List, or the Sectoral Sanctions Identification List, which are all 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.

9. **Brokers**. Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, "**Broker**") in connection with the transaction reflected in this Fifth Amendment and that no Broker brought about this transaction, other than Newmark and CBRE. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than Newmark and CBRE, claiming a commission or other form of compensation by virtue of having dealt with Landlord or Tenant, as applicable, with regard to this Fifth Amendment.

10. **Miscellaneous**.

(a) This Fifth 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 Fifth Amendment may be amended only by an agreement in writing, signed by the parties hereto.

(b) This Fifth Amendment is binding upon and shall inure to the benefit of the parties hereto, and their respective successors and assigns.

(c) This Fifth 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 Fifth 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 Fifth 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 Fifth Amendment. In the event of any conflict between the provisions of this Fifth Amendment and the provisions of the Lease, the provisions of this Fifth Amendment shall prevail. Whether or not specifically amended by this Fifth 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 Fifth Amendment.

(e) Tenant acknowledges that Landlord's business operations are proprietary to Landlord. Absent prior written consent from Landlord, Tenant shall hold confidential and will not disclose to third parties, and shall require Tenant's assignees, sublessees, licensees, agents, servants, employees, invitees and contractors (or any of Tenant's assignees, sublessees and/or licensees respective agents, servants, employees, invitees and contractors) to hold confidential and not disclose to third parties, information regarding the systems, controls, equipment, programming, vendors, tenants, and specialized amenities of Landlord.

[Signatures are on the next page]

IN WITNESS WHEREOF, the parties have caused their duly authorized representatives to execute this Fifth Amendment as of the date first written above.

TENANT:

ULTRAGENYX PHARMACEUTICAL INC.
a Delaware corporation

Approved and Executed by: **/s/ Emil Kakkis**
Name: Emil Kakkis
Its: CEO
Date: November 20, 2024
I hereby certify that the signature, name and title above are my signature, name and title

LANDLORD:

ARE-MA REGION NO. 20, 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, general partner

By: /s/ Scott A. Sherwood
Name: Scott A. Sherwood
Its: Real Estate Legal Affairs
Date: November 25, 2024

EXHIBIT A

FORM OF SHARED SPACE ACKNOWLEDGMENT

This Shared Space Acknowledgment (this "**Acknowledgment**") is made as of , 20 , by and among **ARE-MA REGION NO. 20, LLC**, a Delaware limited liability company ("**Landlord**"), and **ULTRAGENYX PHARMACEUTICAL INC.**, a Delaware corporation ("**Tenant**"), and , ("**Shared Space Occupant**"), with reference to the following Recitals.

R E C I T A L S

A. Landlord and Tenant are now parties to that certain Lease Agreement dated , 2024 (as the same may in the future be amended, the "**Lease**") wherein Tenant leases certain premises consisting of approximately [ ] rentable square feet (the "**Premises**") in the building located at 19 Presidential Way, Woburn, Massachusetts. All initially capitalized terms not otherwise defined in this Acknowledgment shall have the meanings set forth in the Lease unless the context clearly indicates otherwise.

B. Tenant desires to permit Shared Space Occupant to use and occupy a portion of the Premises, as more particularly described in and pursuant to the provisions of that certain [Agreement] dated as of , 20 (the "**Shared Space Agreement**"), a copy of which is attached hereto as Schedule 1.

NOW, THEREFORE, in consideration of the foregoing and the agreements contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto hereby agree as follows:

1. Tenant and Shared Space Occupant each represent and warrant to Landlord that the copy of the Shared Space Agreement attached hereto as Exhibit A is true, correct and complete.

2. The terms of the Shared Space Agreement are subject and subordinate to the terms of the Lease. Landlord shall have no obligations to Shared Space Occupant or any party claiming by or through Shared Space Occupant.

3. If the Lease terminates, then the Shared Space Agreement shall automatically terminate concurrently therewith.

4. All waivers and releases set forth in the Lease that apply as between Landlord and Tenant thereunder shall also apply as between Landlord and Shared Space Occupant.

5. Tenant shall deliver to Landlord a certificate of insurance from Shared Space Occupant, as insured, evidencing no less than the insurance requirements set forth in Section 17 of the Lease concurrent with Tenant's delivery to Landlord of a fully executed copy of this Acknowledgment and prior to the expiration of such policy.

6. Tenant hereby indemnifies and agrees to hold Landlord harmless from and against any loss or liability arising from any commissions or fees payable in connection with the Shared Space Agreement.

7. Notwithstanding anything in the Shared Space Agreement to the contrary, Landlord and Shared Space Occupant each hereby release the other, and waive their respective rights of recovery against the other for direct or consequential loss or damage arising out of or incident to the perils covered by property insurance carried by such party to the extent of such insurance and waive any right of subrogation which might otherwise exist in or accrue to any person on account thereof.

8. Tenant and Shared Space Occupant agree that upon any conflict between the terms of the Shared

Space Agreement and this Acknowledgment, the terms of this Acknowledgment shall control.

9. This Acknowledgment and the legal relations between the parties hereto shall be governed by and construed and enforced in accordance with the internal laws of Commonwealth of Massachusetts, without regard to its principles of conflicts of law.

10.Tenant and Shared Space Occupant are currently (a) in compliance with (and are required to at all times during the term of the Shared Space Agreement to 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 Shared Space Agreement be listed on, the Specially Designated Nationals and Blocked Persons List, Foreign Sanctions Evaders List, or the Sectoral Sanctions Identification List, which are all 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.

11.This Acknowledgment 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 Acknowledgment and all matters related thereto, with such electronic signatures having the same legal effect as original signatures

[Signatures on next page]

IN WITNESS WHEREOF, Tenant and Shared Space Occupant have caused their duly authorized representatives to execute this Acknowledgment as of the date first above written.

TENANT:

ULTRAGENYX PHARMACEUTICAL INC.,
a Delaware corporation

By: Name: Its:

□ I hereby certify that the signature, name, and title above are my signature, name and title.

SHARED SPACE OCCUPANT:

, a

By: Name: Its:

□ I hereby certify that the signature, name, and title above are my signature, name and title.

LANDLORD:

ARE-MA REGION NO. 20, 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, general partner

By: Name: Its

Exhibit 10.89

FOURTH AMENDMENT TO LEASE

THIS FOURTH AMENDMENT TO LEASE (this "**Fourth Amendment**") is made as of December 13, 2024 (the "**Fourth Amendment Effective Date**"), by and between **GI ETS SHORELINE LLC**, a Delaware limited liability company ("**Landlord**"), and **ULTRAGENYX PHARMACEUTICAL INC.**, a Delaware corporation **("Tenant").**

WHEREAS, Landlord (as successor-in-interest to ARE-San Francisco No. 17, LLC) and Tenant are parties to that certain Lease Agreement dated as of December 15, 2019 (the "**Original Lease**"), as amended by that certain First Amendment to Lease Agreement dated as of September 30, 2020 (the "**First Amendment**"), Second Amendment to Lease Agreement as of October 21, 2020 (the "**Second Amendment**"), and Third Amendment to Lease Agreement dated as of July 27, 2022 (the "**Third Amendment**"; and, together with the Original Lease, First Amendment, Second Amendment, and Third Amendment, collectively, the "**Lease**"), demising approximately 32,377 rentable square feet (the "**Premises**") in the building located at 7000 Shoreline Court, South San Francisco, California (the "**Building**");

WHEREAS, the Base Term of the Lease currently expires on March 31, 2025 (the "**Current Expiration Date**") and Tenant has requested that Landlord, among other things, extend the Base Term; and

WHEREAS, Landlord and Tenant desire, subject to the terms and conditions set forth below, to amend the Lease as set forth in this Fourth Amendment.

NOW, THEREFORE, in consideration of the mutual covenants contained herein and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, Landlord and Tenant do hereby agree as follows:

1.**Definitions**. Unless the context otherwise requires, any capitalized or defined term used herein shall have its respective meaning as set forth in the Lease.

2. **Term**.

(a)Base Term. The Base Term is extended to expire on April 30, 2027 (the "**New Expiration Date**").

(b) Extension Term.

(i) Clause (a) of Section 40 of the Lease is hereby deleted in its entirety and replaced with the following:

"(a) Extension Right. Tenant shall have one (1) right (the **"Extension Right**") to extend the term of this Lease for 36 months (the **"Extension Term**") on the same terms and conditions as this Lease (other than with respect to Base Rent and the Work Letter) by giving Landlord written notice (the **"Exercise Notice**") of its election to exercise the Extension Right at least nine (9) months, but not more than fifteen (15) months, prior to the expiration of the current Term of the Lease (the **"Exercise Date**"). Notwithstanding the foregoing, Tenant shall have the right to extend the Term by giving written notice to Landlord of its election to extend less than nine (9) months prior to the expiration of the current Term,

provided that Tenant's notice is accompanied by a payment of (a) one (1) month's Full Service Gross Rent (as hereinafter defined) for each full calendar month that the written notice is delayed, and (b) a prorated daily amount of one (1) month's Full Service Gross Rent for each partial calendar month that the written notice is delayed. For the avoidance of doubt, should Tenant provide Landlord with three (3) months' prior written notice of its election to extend the Term, such notice must be accompanied by Tenant's payment of six (6) months' Full Service Gross Rent. "**Full Service Gross Rent**" shall mean Base Rent plus Tenant's Share of (i) Utilities, (ii) Operating Expenses and (iii) Landlord's insurance policies covering the Project.

Upon the commencement of the Extension Term, Base Rent shall be payable at the Market Rate (as defined below). Base Rent shall thereafter be adjusted on each annual anniversary of the commencement of such Extension Term by a percentage as determined by Landlord and agreed to by Tenant at the time the Market Rate is determined. As used herein, "Market Rate" shall mean the rate that comparable landlords of comparable buildings have accepted in current transactions from non-equity (i.e., not being offered equity in the buildings) and nonaffiliated tenants of similar financial strength for space of comparable size, quality (including all Tenant Improvements, Alterations and other improvements) and floor height in Class A laboratory/office buildings in South San Francisco for a comparable term, with the determination of the Market Rate to take into account all relevant factors, including tenant inducements (including, without limitation, rent abatements and tenant improvement allowances), available amenities (parking costs, leasing commissions, allowances or concessions, if any). Tenant shall exercise the Extension Right, if at all, as follows (i) Landlord shall deliver written notice (the "**Option Rent Notice**") to Tenant within thirty (30) days after Landlord's receipt of Tenant's Exercise Notice setting forth Landlord's good faith determination of the Market Rate, and (ii) Tenant may object, in a writing delivered to Landlord within ten (10) days after Tenant's receipt of the Option Rent Notice (the "**Objection Notice**"), to Landlord's determination of the Market Rate set forth in the Option Rent Notice, in which event such Market Rate shall be determined by arbitration pursuant to Section 40(b) below. If Tenant does not deliver an Objection Notice pursuant to the immediately preceding sentence, Tenant shall be deemed to have accepted the Market Rate set forth in the Option Rent Notice. Tenant acknowledges and agrees that, if Tenant has delivered an Exercise Notice to Landlord pursuant to this Section 40(a), Tenant shall have no right thereafter to rescind such Exercise Notice or elect not to extend the term of the Lease for the Extension Term. For the avoidance of doubt, the Extension Right under this Section 40(a) is not personal to Tenant."

(ii) Clause (c) of Section 40 of the Lease is hereby deleted in its entirety.

(c) Term. The definition of "**Term**" set forth in the Original Lease shall be deleted in its entirety and replaced with the following:

""**Term**" shall mean the Base Term (as extended by this Fourth Amendment to expire on the New Expiration Date), as the same may be extended pursuant to Section 2 of this Fourth Amendment, unless sooner terminated as provided in the Lease (as amended by this Fourth Amendment)."

3.**Base Rent**. Tenant shall continue to pay Base Rent as provided for in the Lease until the Current Expiration Date with respect to the Premises. For the period commencing on the day following the Current Expiration Date through the New Expiration Date, Tenant shall pay Base Rent as follows with respect to the Premises:

	Monthly Base Rent Amount
April 1, 2025 – March 31, 2026	$63,715.71 (Note: During this period, Base Rent is owed only for the first floor space consisting of 10,781 square feet)
April 1, 2026 – March 31, 2027	$197,088.51
April 1, 2027 – April 30, 2027	$203,001.17

Notwithstanding the foregoing, Base Rent shall be abated for the month of April 2025.

Base Rent and all other Rent shall be due and payable as provided under the Lease. For the avoidance of doubt, Tenant shall be responsible for the payment in full of Tenant's Share of Operating Expenses for the period commencing on the day following the Current Expiration Date through the New Expiration Date.

4. **Permitted Use**. The Permitted Use as set forth in the basic lease provisions on Page 1 of the Lease is restated as follows:

> "**Permitted Use**: 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 consistent with first class life science/R&D/office facilities in the Greater San Francisco area, and not conducted by a government, local, state or federal agency, and otherwise in compliance with the provisions of Section 7 hereof."

5.**Tenant Improvement Allowance**. Landlord and Tenant acknowledge and agree that (i) no TI Allowance is available to Tenant under the Lease and (ii) no TI Allowance shall be available to Tenant in connection with this Fourth Amendment.

6. **Taxes**. Tenant acknowledges that Landlord is contesting certain Taxes pursuant to appropriate legal proceedings in accordance with Section 9 of the Lease ("**Tax Contest**"). Landlord shall, upon written request from Tenant, within two (2) business days, make available for Tenant's review a copy of the tax appeal application related to the Tax Contest. In the event that a taxing authority decreases the amount of property taxes owed by Landlord with respect to the Building for a period during which Tenant occupied the Premises, and at the time of the decrease, Tenant is no longer occupying the Premises, Tenant shall be entitled to Tenant's pro rata share (which is the same as Tenant's Share of Operating Expenses) of any refund related to Taxes that accrued while Tenant was occupying the Premises.

7.**Signage**. Section 38 of the Lease is deleted in its entirety and replaced with the following:

"**Signs; Exterior Appearance**. Tenant shall have the right, at Tenant's sole cost and expense and upon receipt of Landlord's prior written approval of the signage to be displayed, such approval in Lender's reasonable discretion, to display signage on decorative plaques inside the main lobby of the Building. Commencing on the Fourth Amendment Effective Date, and throughout any Extension Term, Tenant shall have the exclusive right to install, maintain, repair, operate, and remove, at its sole cost and expense, one (1) sign ("**Tenant's Signage**") on the uppermost façade of the Building (including, without limitation, back lit signage and LED signage (or comparable streaming technology) and other programmable electronic technology, to the extent such signage technology complies with all applicable Legal Requirements), provided that:
(a) Tenant obtains Landlords prior written approval of the design and color of the Tenant Signage, such approval in Lender's reasonable discretion, (b) the location is reasonably agreed upon by Landlord and Tenant following Tenant's delivery of a signage plan which indicates the proposed locations for Tenant's Signage; and (c) Tenant's Signage complies with all applicable laws and zoning restrictions. Tenant's Signage may be sized, at Tenant's discretion, to the maximum specifications allowed by applicable laws and zoning restrictions. Other than Tenant's Signage, Tenant shall not, without the prior written consent of Landlord, which may be granted or withheld in Landlord's sole discretion (i) attach any awnings, exterior lights, decorations, balloons, flags, pennants, banners, painting or other projection to any outside wall of the Project, (ii) use any curtains, blinds, shades or screens other than Landlord's standard window coverings, (iii) coat or otherwise sunscreen the interior or exterior of any windows, (iv) place any bottles, parcels, or other articles on the window sills, (v) place any equipment, furniture or other items of personal property on any exterior balcony, (vi) paint, affix or exhibit on any part of the Premises or the Project any signs, notices, window or door lettering, placards, decorations, or advertising media of any type which can be viewed from the exterior of the Premises or (vii) place any items on the exterior of corridor walls or corridor doors, other than Landlord's standard lettering. For purposes of clarification, the Fourth Amendment Effective Date timing restriction shall apply only to the actual installation of Tenant's Signage; and Tenant shall be entitled to obtain Landlord's prior written approval and/or any required permits and approvals prior to the Fourth Amendment Effective Date. Tenant shall not be responsible for the payment of any signage rent, or other form of signage fee, to Landlord for Tenant's Signage. For the avoidance of doubt, rights under this Section 38 are not personal to Tenant."

8.**Subordination**. Section 27 of the Lease is deleted in its entirety and replaced with the following:

"**Subordination**. This Lease and Tenant's interest and rights hereunder are hereby made and shall be subject and subordinate at all times to the lien of any Mortgage now existing or hereafter created on or against the Project or the Premises, and all amendments, restatements, renewals, modifications, consolidations, refinancing, assignments and extensions thereof, without the necessity of any further instrument or act on the part of Tenant, provided, however that so long as there is no Default hereunder, Tenant's right to possession of the Premises pursuant to the terms of the Lease (as amended) shall not be disturbed by the Holder of any such Mortgage. Tenant agrees, at the election of the Holder of any such Mortgage, to attorn to any such Holder. Tenant agrees upon demand to execute, acknowledge and deliver such instruments, confirming such subordination, and such

instruments of attornment as shall be requested by any such Holder, provided any such instruments contain appropriate non-disturbance provisions assuring Tenant's quiet enjoyment of the Premises as set forth in Section 24 hereof. Following the Fourth Amendment Effective Date, Landlord shall use commercially reasonable efforts to deliver to Tenant a subordination, non-disturbance and attornment agreement from any the Holder of any Mortgage or any other superior interest holder of the Project. Notwithstanding the foregoing, any such Holder may at any time subordinate its Mortgage to this Lease, without Tenant's consent, by notice in writing to Tenant, and thereupon this Lease shall be deemed prior to such Mortgage without regard to their respective dates of execution, delivery or recording and in that event such Holder shall have the same rights with respect to this Lease as though this Lease had been executed prior to the execution, delivery and recording of such Mortgage and had been assigned to such Holder. Landlord shall deliver to Tenant a copy of any default notice relating to the Project or the Premises received by Landlord, within thirty (30) business days of Landlord's receipt of such default notice, from any Holder of any Mortgage, ground lessor or from a governmental agency. The term **"Mortgage"** whenever used in this Lease shall be deemed to include deeds of trust, security assignments and any other encumbrances, and any reference to the **"Holder"** of a Mortgage shall be deemed to include the beneficiary under a deed of trust."

9. **Security Deposit.** The Security Deposit as set forth in the basic lease provisions on Page 1 of the Lease is restated as follows:

> "**Security Deposit**: As of the Fourth Amendment Effective Date: $108,888.10. Within thirty (30) days of the Fourth Amendment Effective Date, the Security Deposit held by Landlord will be decreased to $54,444.05."

10. **Parking**. The second sentence of Section 10 of the Lease is deleted in its entirety and replaced with the following:

> "Tenant's pro rata share of parking shall be equal to 3.3 parking spaces per 1,000 rentable square feet of the Premises."

11. **Artificial Intelligence and Corporate Spying**. The following is added to the end of Section 42(c) of the Lease:

"Landlord shall not use Generative AI Technology (as hereinafter defined) in connection with the processing of Tenant's financial information without obtaining Tenant's prior written consent, such consent not to be unreasonably withheld, conditioned or delayed. In the event Tenant's prior written consent is obtained, the technology provider must maintain human oversight and accountability over all uses of Generative AI Technology in connection with the processing of Tenant's financial information, to ensure outputs are accurate and free from bias. For purposes of this Lease, (a) "**AI Technology**" means any and all machine learning, deep learning, and other artificial intelligence ("AI") technologies, including statistical learning algorithms, models (including large language models), neural networks, and other AI tools or methodologies, all software implementations of any of the foregoing, and related hardware or equipment, and (b) "**Generative AI Technology**" means AI Technology that generates content."

12. **Restoration and Removable Installations**.[1] Exhibit F of the Original Lease (as amended by Exhibit D attached to the First Amendment) is hereby deleted and amended, restated and replaced in its entirety with the "Exhibit F" attached hereto as Exhibit A to this Fourth Amendment, which shall list the Removable Installations which Tenant shall be entitled to remove following the expiration or earlier termination of the Lease.

13. **Quiet Enjoyment**. Section 24 of the Lease is deleted in its entirety and replaced with the following:

"**Quiet Enjoyment**. So long as Tenant is not in Default under this Lease, Tenant shall, subject to the terms of this Lease, at all times during the Term, have peaceful and quiet enjoyment of the Premises against (i) any person claiming by, through or under Landlord, and (ii) any surveillance by camera within the Premises. Landlord shall use commercially reasonable efforts to cause any service providers engaged by Landlord that enter the Premises to comply with this provision. Further, Landlord agrees to reasonably cooperate with Tenant should Tenant pursue any reasonable request for removal of a service provider in furtherance of its right to privacy."

14. **Binding Effect; Ratification; Conflict**. This Fourth Amendment shall be binding upon the parties and their respective successors and assigns. Except as modified by this Fourth Amendment, all of the terms and conditions of the Lease shall remain unmodified and in full force and effect. To the extent the terms and conditions of the Lease conflict with or are inconsistent with this Fourth Amendment, the terms and conditions of this Fourth Amendment shall control.

15. **Authority**. Tenant hereby represents and warrants that (a) Tenant is in good standing under the laws of the state in which the Building is located, (b) Tenant has full power and authority to enter into this Fourth Amendment and to perform all Tenant's obligations under this Fourth Amendment, and (c) each person (and all of the persons if more than one signs) signing this Fourth Amendment on behalf of Tenant is duly and validly authorized to do so.

16. **No Offer**. Submission of this Fourth Amendment for examination and signature to Tenant does not constitute an offer to amend the Lease, and this instrument is not effective as an amendment to the Lease or otherwise until executed and delivered by both Landlord and Tenant.

17. **Brokers**. Landlord and Tenant each represents and warrants to the other that they have not dealt with any broker in connection with this Fourth Amendment, other than Jones Lang LaSalle (as Landlord's representative) and Kidder Mathews of California ("**Tenant's Representative**"). Landlord and Tenant each agrees to defend, indemnify and hold the other harmless from and against all claims by any other broker for fees, commissions or other compensation to the extent such broker alleges to have been retained by the indemnifying party in connection with the execution of this Fourth Amendment. Landlord shall pay Tenant's Representative in accordance with that certain Kidder – Commission Agreement, dated as of May 21, 2024, by and between Landlord and Tenant's Representative.

18. **Entire Agreement**. This Fourth Amendment, together with the Lease, constitutes the entire agreement between Landlord and Tenant regarding the Lease and the subject matter

[1] NTD: Tenant to provide proposed Exhibit A (removable installations).

contained herein and supersedes any and all prior and/or contemporaneous oral or written negotiations, agreement or understandings, except as otherwise expressly provided herein. This Fourth Amendment may not be amended or modified except pursuant to a written instrument executed by both Landlord and Tenant.

19. **Attorneys' Fees**. Should any suit be brought to enforce or interpret the terms of this Fourth Amendment or any obligation herein, the prevailing party, either by way of settlement or by final judgment, shall be entitled to recover its reasonable out-of-pocket attorneys' fees, costs and expenses.

20. **Construction**. The headings used in this Fourth Amendment are for convenience and reference use only, and are not to be considered in the construction or interpretation of this Fourth Amendment. The parties agree that each party and its legal counsel has reviewed or has had the opportunity to review this Fourth Amendment and that any rule of construction to the effect that ambiguities are to be resolved against the drafting party shall not apply in any construction or interpretation of this Fourth Amendment.

21. **Governing Law**. This Fourth Amendment shall be construed and enforced in accordance with the laws of the state in which the Building is located applicable to contracts entered into in such state by parties residing therein.

22. **Counterparts; Electronic Delivery**. This Fourth Amendment may be executed in counterparts, each of which shall be deemed a part of an original and all of which together shall constitute one (1) agreement. Signature pages may be detached from the counterparts and attached to a single copy of this Fourth Amendment to form one (1) document. Furthermore, this Fourth Amendment may be executed and delivered by electronic transmission. The parties intend that electronic (e.g. pdf format or DocuSign) signatures constitute original signatures and that an electronic copy or counterparts of this Fourth Amendment containing signatures (original or electronic) of a party is binding upon that party.

23. **Invalidity**. If any provision of this Fourth Amendment is invalid or unenforceable under applicable law, such invalidity or unenforceability shall not affect the validity and enforceability of the remaining provisions of this Fourth Amendment.

IN WITNESS WHEREOF, Landlord and Tenant have executed this Fourth Amendment as of the day and year first written above.

LANDLORD: **TENANT**:

GI ETS SHORELINE LLC,
a Delaware limited liability company

Approved and Executed By:

By: /s David Boehle
Name: David Boehle
Title: Director

ULTRAGENYX PHARMACEUTICAL INC.,
a Delaware corporation

Approved and Executed By:
/s/ Emil Kakkis
Name: Emil Kakkis
Title: Chief Executive Officer

Exhibit 10.93

FIRST AMENDMENT TO LEASE

This First Amendment to Lease (this "Amendment") is made and entered into as of March 12, 2024, by and 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").

W I T N E S S E T H:

WHEREAS, Landlord and Tenant are parties to a Lease dated August 18, 2022 (the "Lease"), whereby Tenant leases from Landlord certain premises (the "Premises") in the building located at 100 Chestnut Street, Somerville, Massachusetts (the "Building"), as more particularly described in the Lease; and

WHEREAS, Landlord and Tenant desire to amend the Lease to provide for the performance of certain additional improvements by Landlord and the temporary increase in the number of parking spaces provided to Tenant, subject to and upon the terms and conditions hereinafter provided.

NOW, THEREFORE, in consideration of the foregoing and for other consideration the mutual receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant agree that the Lease is hereby amended as follows:

1.Unless otherwise defined herein, all capitalized terms shall have the same meaning as they have been assigned in the Lease.

2.Landlord shall, not later than April 30, 2024, and at Landlord's sole cost and expense, install a Building-standard WiFi/LTE booster or extender at the Building.

3.The third paragraph of Section 3.3(c) of the Lease is hereby amended by inserting the following as the third sentence thereof:

> Notwithstanding anything herein to the contrary, the hard costs of Tenant's Work shall not include the first Ninety Thousand and 00/100 Dollars ($90,000.00) of the costs of Tenant's Work in excess of the Maximum Turnkey Amount.

4.The second sentence of the second paragraph of Section 3.6 of the Lease is hereby deleted and in its place the following shall be inserted:

> If the Total TI Costs exceed the Maximum Turnkey Amount, Landlord shall pay the first Ninety-Thousand and 00/100 Dollars ($90,000.00) of such excess and 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.

5.Tenant shall be entitled to a credit in the amount of Forty-Two Thousand and 00/100 Dollars ($42,000.00), which credit shall be applied in equal monthly installments between April 1, 2024, and December 31, 2024, in the amount of Four Thousand Six Hundred Sixty-Six and 67/100 Dollars ($4,666.67) per month. At Tenant's election, such credit shall be applied to charges incurred by Tenant at the café located in the Building.

6.This Amendment 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.

7. As amended hereby, the Lease is hereby ratified and confirmed.

[Signature Page to Follow]

IN WITNESS WHEREOF, the parties hereunto have executed this Amendment as of the date first written above.

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
13-March-2024

TENANT:

Ultragenyx Pharmaceutical Inc.

By: /s/ Emil Kakkis
Name: Emil Kakkis
Title: CEO
12-March-2024

Exhibit 19.1

ULTRAGENYX PHARMACEUTICAL INC.

INSIDER TRADING POLICY
Approved: March 15, 2023

This Insider Trading Policy (this "Policy") applies to all employees, officers, directors and consultants of Ultragenyx Pharmaceutical Inc. and its subsidiaries (collectively, the "Company") as well as your family members, household members and entities controlled by you (as described below). This Policy is designed to prevent insider trading or allegations of insider trading, and to protect the Company's reputation for integrity and ethical conduct. It is your obligation to understand and comply with this Policy. Should you have any questions regarding this Policy, please contact the Company's Chief Financial Officer ("CFO") or the Company's Chief Legal Officer.

BACKGROUND

The Company's Board of Directors (the "Board") has adopted this Policy for our directors, officers, employees, and consultants as well as their family members, household members and entities controlled by them (as described below) with respect to the trading of the Company's securities, as well as the securities of publicly traded companies with whom we have a business relationship.

Federal and state securities laws prohibit the purchase or sale of a company's securities by persons who are aware of material information about that company that is not generally known or available to the public. These laws also prohibit persons who are aware of such material nonpublic information from disclosing this information to others who may trade. Companies and their controlling persons are also subject to liability if they fail to take reasonable steps to prevent insider trading by company personnel.

It is important that you understand the breadth of activities that constitute illegal insider trading and the consequences for such activities, which can be severe. Both the U.S. Securities and Exchange Commission (the "SEC") and The Nasdaq Stock Market LLC ("Nasdaq") investigate and are very effective at detecting insider trading. The SEC, together with the Offices of the U.S. Attorneys, pursues insider trading violations vigorously. Cases have been successfully prosecuted against trading by employees through foreign accounts, trading by family members and friends, and trading involving only a small number of shares.

PENALTIES FOR NONCOMPLIANCE WITH THIS POLICY

The Law. Federal law imposes heavy penalties on those who, in violation of law, either buy or sell securities while aware of material nonpublic information, or pass such material nonpublic information along to others who use it to buy or sell securities (known as “tipping”).

Civil and Criminal Penalties. Potential penalties for insider trading violations include (1) imprisonment for up to 20 years, (2) criminal fines of up to $5 million, and (3) civil fines of up to three times the profit gained or loss avoided.

Controlling Person Liability. If the Company fails to take appropriate steps to prevent illegal insider trading, the Company may have “controlling person” liability for a trading violation, with civil penalties of up to the greater of (1) $1.525 million, as may be adjusted for inflation, and (2) three times the profit gained or loss avoided, as well as a criminal penalty of up to $25 million. The civil penalties can extend personal liability to the Company’s directors, officers, and other supervisory personnel if they fail to take appropriate steps to prevent insider trading.

Company Sanctions. Failure to comply with this Policy may also subject you to Company-imposed sanctions, including dismissal for cause, whether or not your failure to comply with this Policy results in a violation of law.

Any of these consequences, and even an investigation that does not result in prosecution, can tarnish the Company’s reputation and irreparably damage you and the Company.

SCOPE OF POLICY

Persons Covered. As a director, officer, employee, or consultant of the Company, this Policy applies to you. The same restrictions that apply to you apply to: (1) your family members who reside with you, (2) anyone else who lives in your household, (3) any family members who do not live in your household but whose transactions in Company securities are directed by you or are subject to your influence or control (such as parents or children who consult with you before they trade in Company securities), (4) any corporations or other business entities controlled or managed by you, and (5) any trusts of which you are the trustee or otherwise have investment control over or beneficial or pecuniary interest. You are responsible for making sure that the purchase or sale of any security covered by this Policy by any such person or entity complies with this Policy.

Companies Covered. The prohibition on insider trading in this Policy is not limited to trading in the Company’s securities. It includes trading in the securities of other companies with whom we have a business relationship such as customers or suppliers of the Company and those with which the Company may be negotiating major transactions, such as an acquisition, investment, or sale. Information that is not material to the Company may nevertheless be material to one of those other companies.

Transactions Generally Covered. Trading includes acquisitions/purchases and dispositions/sales of stock, derivative securities (such as put and call options and convertible debentures or

preferred stock), debt securities (debentures, bonds, and notes), and gifts of securities. Trading also includes entering into or modifying a 10b5-1 Plan (as defined below) to trade securities in the future. Trading also includes certain transactions under Company plans, but not all of such transactions are subject to the trading restrictions under this Policy. Specifically:

- *Stock Option Exercises and Restricted Stock/RSU Vesting.* This Policy's trading restrictions generally do not apply to the exercise of a stock option (whether in cash or through a net exercise). The trading restrictions do apply, however, to any sale of the underlying stock or to a cashless exercise of the option through a broker, as this entails selling a portion of the underlying stock to cover the costs of exercise. In addition, this Policy's restrictions do not apply to the withholding of shares by the Company to satisfy a tax withholding obligation upon the vesting of restricted stock or settlement of restricted stock units (if applicable, and to the extent permitted under the Company's equity incentive plans). However, the sale of shares, including a broker-assisted cashless exercise, to satisfy tax withholding obligations is subject to the restrictions set forth in this Policy.

- *Employee Stock Purchase Plan*. This Policy also does not apply to your purchases of Company stock in the Company's Employee Stock Purchase Plan (the "ESPP") resulting from your periodic contribution of money to the ESPP pursuant to your payroll deduction election that is made while you are permitted to trade under this Policy and you are not aware of material nonpublic information regarding the Company. However, this Policy will apply to any: (a) election to participate in the ESPP for an enrollment period; (b) election to increase or decrease your amount of periodic contributions to the ESPP; and (c) sales of Company stock purchased under the ESPP.

Transaction Not Covered. If you own shares of a mutual fund that invests in the Company's securities, there are no restrictions on trading the shares of the mutual fund at any time.

STATEMENT OF POLICY

No Trading on Material Nonpublic Information. You may not trade in the securities of the Company, directly or indirectly, including through family members or other persons or entities, if you are aware of any material nonpublic information relating to the Company. Similarly, you may not trade, directly or indirectly, in the securities of any other company with whom we have a business relationship if you are aware of material nonpublic information about that company, including material nonpublic information that you obtained in the course of your employment with the Company.

As described below, directors, certain officers and designated employees as well as their family members, household members and entities under their control may only trade in Company securities during specific periods each quarter. The Company will notify you if you are subject to these trading restrictions. From time to time due to certain developments relating to

material nonpublic information, the Company may also implement special blackout periods during which the Company may notify all employees or particular individuals that they should not engage in any transactions involving the purchase or sale of Company securities or the securities of another company. If you are subject to a special blackout period, you should not trade in the applicable company's securities during such time and you should not disclose to others the fact that you are prohibited from trading. However, it is not the Company's policy to impose special blackout periods every time that material nonpublic information exists, or every time that a Company employee may be in the possession of material nonpublic information. Thus, the absence of a special blackout should not be interpreted as permission to trade.

In addition, is it the Company's policy to comply with all applicable securities laws when issuing or repurchasing its securities.

No Tipping. You may not pass material nonpublic information of the Company or any other company on to others or recommend to anyone the purchase or sale of any securities of the Company or any such other company when you are aware of such information. This practice, known as "tipping," also violates the securities laws and can result in the same civil and criminal penalties that apply to insider trading, even though you did not trade and did not gain any benefit from another's trading.

No Exception for Hardship. The existence of a personal financial emergency does not excuse you from compliance with this Policy.

DEFINITION OF MATERIAL NONPUBLIC INFORMATION

Note that material nonpublic information has two important elements: (1) materiality and (2) public availability.

Material Information. Information is material if there is a substantial likelihood that a reasonable investor would consider it important in deciding whether to buy, hold, or sell a security. Any information that could reasonably be expected to affect the price of the security is material. Common examples of material information are:

- earnings or losses and other financial information, including projections or other earnings guidance, whether or not they are significantly higher or lower than generally expected by the investment community;
- a pending or proposed merger, acquisition, or sale of all or part of the Company's business;
- current, proposed or contemplated transactions, business plans, financial restructurings, acquisition targets or significant expansions or contractions of operations;
- impending securities offerings by the Company;
- changes in management, directors or auditors;
- clinical trial results;

- significant new products or discoveries;
- negotiations regarding an important license, distribution agreement, or joint venture;
- pending FDA or other regulatory action;
- major events regarding the Company's securities, including the declaration of a stock split, dividend or the offering of additional securities;
- impending financial problems;
- actual or threatened major litigation, or the resolution of such litigation;
- significant actual or potential cybersecurity incidents or events that affect the Company or third party providers that support the Company's business operations, including computer system or network compromises, viruses or other destructive software, and data breach incidents that may disclose personal, business or other confidential information;
- new major contracts, order, suppliers, customer or finance sources, or the loss thereof; or
- changes in the status of any of the Company's activities which may have an adverse or favorable impact.

Note that other types of information may also be material; no complete list can be given.

Both positive and negative information can be material. Because trading that receives scrutiny from federal and Nasdaq investigators will be evaluated after the fact with the benefit of hindsight, when in doubt, questions concerning the materiality of particular information should be resolved in favor of considering it material, and trading should be avoided.

Nonpublic Information. Nonpublic information is information that is not generally known or available to the public. One common misconception is that material information loses its "nonpublic" status as soon as a press release is issued disclosing the information. In fact, information is considered to be available to the public only when it has been released broadly to the marketplace (such as by a press release or an SEC filing) *and the investing public has had time to absorb the information fully.* As a general rule, Company information is considered nonpublic until after the second full trading day after the information is released. For example, if the Company announces financial earnings before trading begins on a Tuesday, the first time you can buy or sell Company securities is the opening of the market on Thursday (assuming you are not aware of other material nonpublic information at that time). However, if the Company announces earnings after trading begins on that Tuesday, the first time you can buy or sell Company securities is the opening of the market on Friday.

EXCEPTION FOR TRANSACTIONS PURSUANT TO RULE 10b5-1 PLANS

An exception to this rule is trading in compliance with Rule 10b5-1 under the Securities Exchange Act of 1934, as amended (the "Exchange Act") pursuant to a contract, instruction, or written plan that (1) specifies, or includes a written formula or algorithm or computer program for determining, the amount, price and date of securities to be purchased or sold, (2) is

established at a time when you were not aware of material, nonpublic information, and (3) satisfies Exchange Act Rule 10b5-1(c) (a “10b5-1 Plan”). Any 10b5-1 Plan is required to be reviewed and approved by the CFO and the Chief Legal Officer, or designees of such persons, prior to entry into such plan. In addition, all amendments, modifications and terminations of a 10b5-1 Plan must be reviewed and approved by the CFO and the Chief Legal Officer, or designees of such persons prior to effecting any such amendments, modifications or terminations. In accordance with SEC rules, any 10b5-1 Plan must also satisfy the following requirements:

- *Timing*. A Rule 10b5-1 Plan can only be entered into, amended, modified or terminated during the Window Period (as defined below) and at a time when the person entering into the plan is not aware of material nonpublic information.

- *Cooling-off Period*. The first scheduled transaction in an approved and executed 10b5-1 Plan must not take place until the end of a cooling-off period, which means (a) if you are a director or Section 16 Executive Officer (defined below), the later of (i) ninety (90) calendar days after the 10b5-1 Plan is entered into, and (ii) two business days following the disclosure of the Company’s financial results in a Form 10-K or Form 10-Q for the fiscal quarter in which the 10b5-1 Plan was adopted (in any case, the transaction may occur after 120 calendar days after the 10b5-1 Plan is entered into), or (b) if you are not a director or Section 16 Executive Officer, thirty (30) calendar days after the 10b5-1 Plan is entered into. Amendments or modifications of a 10b5-1 Plan that impact the amount, price or timing of transactions under the plan will be treated as the adoption of a new plan and subject to the applicable cooling-off period described above.

- *Good Faith*. The 10b5-1 Plan must be entered into in good faith and not as part of a plan or scheme to evade the prohibitions of the securities laws, and you must act in good faith with respect to the 10b5-1 Plan.

- *Restrictions on Overlapping and Single-Trade Plans*. You may not enter into more than one 10b5-1 Plan for trading Company securities during the same period, unless the additional plan only authorizes “sell-to-cover” transactions to satisfy tax withholding obligations in connection with the vesting of equity awards. In addition, you may not enter into more than one single-trade 10b5-1 Plan within a 12-month period.

Directors and Section 16 Executive Officers are subject to additional requirements when entering into 10b5-1 Plans, including certification requirements (regarding material non-public information and good faith) as well as disclosure requirements (e.g., the Company will need to disclose in its Form 10-Q or Form 10-K the material terms of your plan, other than price).

In accordance with SEC rules, any 10b5-1 Plan adopted prior to February 27, 2023 that is not subsequently modified or amended on or after February 27, 2023 in the manner described under “Cooling-off Period” above is grandfathered from certain of the requirements described

in this section. Please contact the Chief Legal Officer with any questions with respect to the requirements applicable to such 10b5-1 Plans.

Other than transactions pursuant to 10b5-1 Plans, there is no exception to this Policy, including for transactions that may be necessary or justifiable for independent reasons (such as the need to raise money for an emergency expenditure, as noted above).

SPECIAL RESTRICTIONS FOR DIRECTORS, SECTION 16 EXECUTIVE OFFICERS AND CERTAIN OTHER PERSONS

Persons Subject to Special Restrictions. To help prevent inadvertent violations of the federal securities laws and to avoid even the appearance of trading on the basis of material nonpublic information, the Board has adopted certain procedures that apply to directors, officers subject to Section 16 of the Exchange Act ("Section 16 Executive Officers"), and certain designated employees and consultants of the Company and its subsidiaries who have access to material nonpublic information about the Company. The Company will notify you if you (as well as your family members, household members and entities you control) are subject to these special trading and/or pre-clearance restrictions, described below.

Window Periods. Each director, Section 16 Executive Officer, certain designated finance team members of the Company, and anyone else specifically designated as subject to window period restrictions may only trade in Company securities from the date that is two full trading days after the Company's filing of a Form 10-Q or Form 10-K with the SEC to the end of business on the Monday of the second full calendar week prior to the end of each quarter (such period, the "Window Period").

However, even if the Window Period is open, you (as well as your family members, household members and controlled entities) may not trade in Company securities if you are aware of material nonpublic information about the Company. In addition, if you are subject to the Company's pre-clearance policy, described below, you must pre-clear transactions even if you (or your family members, household member or controlled entity) initiate them when the Window Period is open.

From time to time during the Window Period, the Company may close trading due to developments (such as a significant event or transaction) that may involve material nonpublic information. In such cases, the CFO and the Chief Legal Officer may notify particular individuals that they should not engage in any transactions in the Company's securities, and should not disclose to others the fact that trading has been prohibited.

Even if the Window Period is closed, you may exercise stock options if no shares are to be sold. However, you may not effect sales of stock issued upon the exercise of stock options (including same-day sales and cashless exercises). Generally, all pending purchase and sale orders regarding Company securities that could be executed while the Window Period is open must be cancelled before it closes.

In light of these restrictions, if you anticipate the need to sell Company stock at a specific time in the future, you may wish to consider entering into a 10b5-1 Plan, as discussed above.

Pre-Clearance Procedures. Each director, Section 16 Executive Officer, certain designated finance team members of the Company, if any, and anyone else specifically designated as subject to pre-clearance restrictions must contact the CFO and the Chief Legal Officer, or designees of such persons in advance of effecting any transaction in the Company's securities and obtain his/her prior approval of the transaction. The pre-clearance policy applies to these individuals (as well as their family members, household members and controlled entities) even if they are initiating a transaction while the Window Period is open. All requests must be submitted at least forty-eight (48) hours prior to making any transaction (purchase or sale) involving the Company's securities. The CFO and the Chief Legal Officer, or designees of such persons will then determine whether the transaction may proceed. If the transaction is approved, the transaction must be executed within five business days after approval is obtained, but regardless may not be executed if you acquire material nonpublic information concerning the Company prior to the transaction's execution. If a transaction is not completed within the period described above, the transaction must be approved again before it may be executed. If a proposed transaction is not approved under the pre-clearance policy, you (or your family member, household member or controlled entity) should refrain from initiating any transaction in Company securities, and you should not inform anyone within or outside the Company of the restriction.

Section 16 Reporting. For directors and Section 16 Executive Officers, if the Company pre-clears the transaction and you proceed with it, the Company will assist you in complying with your reporting obligations under Section 16 of the Exchange Act ("Section 16"). Under Section 16, directors and Section 16 Executive Officers are required to a file a Form 4 within two business days after certain changes in beneficial ownership occur (including the exercise of options or other derivative securities and gifts of securities). Form 4 requires that you provide detailed information relating to any purchase, sale, or exercise, including the price of the shares acquired or disposed, the transaction date, and the amount of securities beneficially owned following the transaction. As such, you should promptly report the details of any transaction that you engage in to the CFO or the Chief Legal Officer.

Rule 144. If you are a director or Section 16 Executive Officer, you may be deemed to be an "affiliate" of the Company. Consequently, shares of Company common stock held by you may be considered to be "restricted securities" or "control securities," the sale of which are subject to compliance with Rule 144 under the Securities Act of 1933, as amended (or any other applicable exemption under the federal securities laws). If this is the case, note that Rule 144 places limits on the number of shares you may be able to sell and provides that certain procedures must be followed before you can sell shares of Company stock. Contact the Chief Legal Officer for more information on Rule 144.

ADDITIONAL GUIDANCE

The Company considers it improper and inappropriate for those employed by or associated with the Company to engage in short term or speculative transactions in the Company's securities or in other transactions in the Company's securities that may lead to inadvertent violations of the insider trading laws. Accordingly, trading in Company securities is subject to the following additional guidance.

Short-term Trading. Any person or entity covered by this Policy may not sell Company securities within six months of purchasing Company securities.

Short Sales. Any person or entity covered by this Policy may not engage in short sales of the Company's securities (sales of securities that are not then owned), including any "sales against the box" (a sale with delayed delivery).

Hedging Transactions. The Company prohibits purchasing "hedge" instruments and engaging in other hedging, offsetting and monetization transactions that are designed to hedge, offset or transfer, with respect to equity compensation received by a director, officer, or employee or other equity securities held (directly or indirectly) by a director, officer or employee, all or a portion of the risk of a decline in the market price of shares of Company securities. Instruments that would be considered to be a "hedge" include prepaid variable forward contracts, equity swaps, collars, and exchange funds. For the avoidance of doubt, 10b5-1 Plans providing for future sales or purchases of securities are not prohibited by this Policy.

Publicly Traded Options and Other Derivative Securities. Any person or entity covered by this Policy may not engage in transactions in publicly traded options on Company securities, such as puts, calls, and other derivative securities, on an exchange or in any other organized market.

Standing Orders. Standing orders should be used only for a very brief period of time. A standing order placed with a broker to sell or purchase stock at a specified price leaves you without control over the timing of the transaction. A standing order transaction executed by the broker when you (or your family member, household member or controlled entity) are aware of material nonpublic information may result in unlawful insider trading.

Margin Accounts and Pledges. Securities held in a margin account or pledged as collateral for a loan may be sold without your consent by the broker if you fail to meet a margin call or by the lender in foreclosure if you default on the loan. A margin or foreclosure sale that occurs when an insider is aware of material nonpublic information may, under some circumstances, result in unlawful insider trading. Because of this danger, you are prohibited from holding Company securities in a margin account or pledging Company securities as collateral for a loan.

POST-TERMINATION TRANSACTIONS

This Policy continues to apply to your transactions in Company securities even after you have terminated employment or other services to the Company or a subsidiary as follows: if you are

aware of material nonpublic information when your employment or service relationship terminates, you may not trade in Company securities until that information has become public or is no longer material.

UNAUTHORIZED DISCLOSURE

Maintaining the confidentiality of Company information is essential for competitive, security, and other business reasons, as well as to comply with securities laws. You should treat all information you learn about the Company or its business plans in connection with your employment as confidential and proprietary to the Company. Inadvertent disclosure of confidential or material nonpublic information may expose the Company and you to significant risk of investigation and litigation.

The timing and nature of the Company's disclosure of material information to outsiders is subject to legal rules, the breach of which could result in substantial liability to you, the Company, and its management. Accordingly, it is important that responses to inquiries about the Company by the press, investment analysts, or others in the financial community be made on the Company's behalf only through authorized individuals. If you receive inquiries of this nature, refer them to the CFO and the Chief Legal Officer.

PERSONAL RESPONSIBILITY

You should remember that the ultimate responsibility for adhering to this Policy and avoiding improper trading rests with you. If you violate this Policy, the Company may take disciplinary action, including dismissal for cause.

COMPANY ASSISTANCE

Your compliance with this Policy is of the utmost importance both for you and for the Company. If you have any questions about this Policy or its application to any proposed transaction, you may obtain additional guidance from the CFO and the Chief Legal Officer. Do not try to resolve uncertainties on your own, as the rules relating to insider trading are often complex, not always intuitive, and carry severe consequences. On an annual basis, you must certify that you have read and understood this Policy.

Exhibit 21.1

Significant Subsidiaries of Ultragenyx Pharmaceutical Inc.

Name of Subsidiary	Jurisdiction of Incorporation
Ultragenyx Holdco LLC	Delaware
Rare Delaware Inc.	Delaware
Amlogenyx Inc.	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
Ultragenyx Chile Limitada	Chile

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, 333-262751, 333-269840, 333-272518, and 333-280776) pertaining to the 2011 Equity Incentive Plan, as amended, 2014 Incentive Plan, as amended, 2014 Employee Stock Purchase Plan, as amended and restated, 2023 Incentive Plan, as amended and restated, and Employee Inducement Plan, as amended 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. 333-277226) 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 19, 2025, 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, 2024.

/s/ Ernst & Young LLP

San Mateo, California
February 19, 2025

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 19, 2025

/s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Howard Horn, 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:

1. 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;

2. 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;

3. 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

4. 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):

1. 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

2. 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 19, 2025

/s/ Howard Horn
Howard Horn
Executive Vice President, Chief Financial Officer, Corporate Strategy (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, 2024 (the "Report"), I, Emil D. Kakkis, M.D., Ph.D., as President and Chief Executive Officer of the Company, and Howard Horn, as Executive Vice President, Chief Financial Officer, Corporate Strategy 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 19, 2025

/s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: February 19, 2025

/s/ Howard Horn
Howard Horn
Executive Vice President, Chief Financial Officer,
Corporate Strategy (Principal Financial Officer)