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 ☐ NO ☑

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☑ NO ☐

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☑

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 $3.7 billion, based upon the closing price on The Nasdaq Global Select Market reported for such date. Shares of common stock held by each executive officer and director and by each person who is known to own 10% or more of the outstanding common stock have been excluded 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.

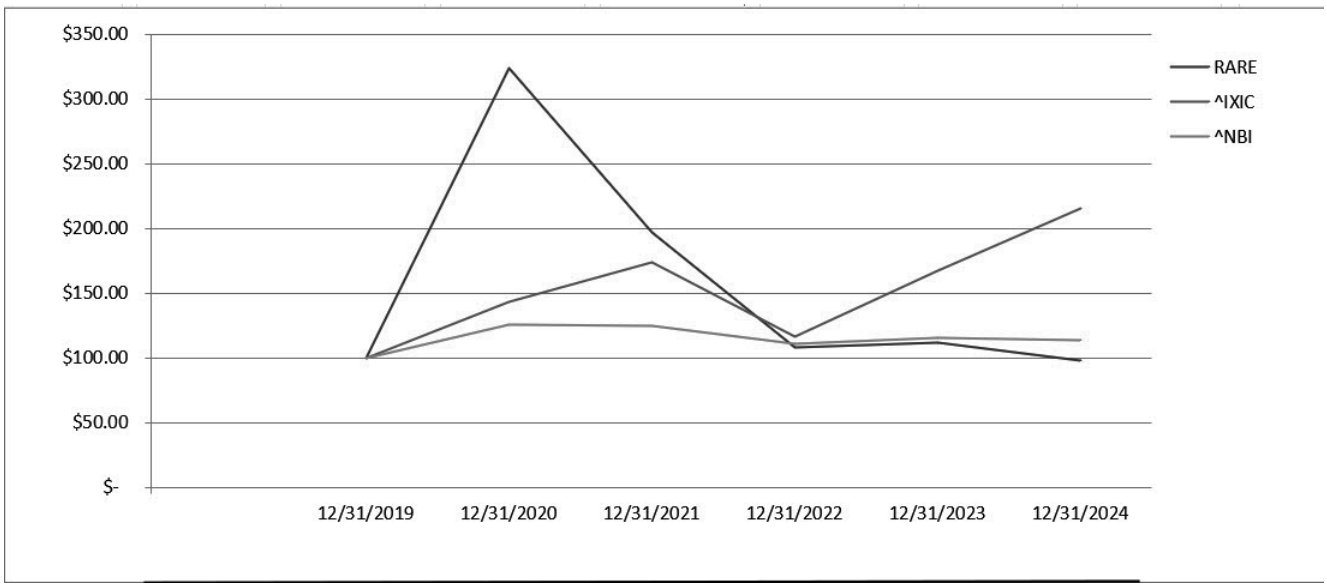
PART II

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,		Dollar	Percent
	2024	2023	Change	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,		Dollar	Percent
	2024	2023	Change	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,		Dollar	Percent
	2024	2023	Change	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,		Dollar	Percent
	2024	2023	Change	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,		Dollar	Percent
	2024	2023	Change	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,		Dollar	Percent
	2024	2023	Change	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,		Dollar	Percent
	2024	2023	Change	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,		Dollar	Percent
	2024	2023	Change	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,		Dollar	Percent
	2024	2023	Change	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 Adopted	Aggregate Number of Shares of Common Stock to be Sold (Subject to Certain Conditions)	Plan End Date
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	10-Q	8/2/2019	10.1	

	Pharmaceutical Inc. and Kyowa Kirin Co., Ltd. (formerly, Kyowa Hakko Kirin Co., Ltd.)				
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 in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's process of accounting for the liabilities related to the sale of future royalties, including controls over the Company's estimates of projected sales of Crysvita in the European and North American markets.

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)
Deferred compensation obligation	3,593	432
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	Accumulated	Treasury	Deferred Compensation	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	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.

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	Gross Unrealized 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):

		December 31,	
	Useful life (years)	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, none 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

ultragenyx

2025 PROXY STATEMENT

May 15, 2025

9:00 a.m. Pacific Time

www.virtualshareholdermeeting.com/RARE2025

60 Leveroni Court
Novato, California 94949

Notice of Annual Meeting of Stockholders

To Be Held on May 15, 2025 at 9:00 a.m. Pacific Time

Dear Stockholder:

You are cordially invited to attend the Annual Meeting of Stockholders of Ultragenyx Pharmaceutical Inc., a Delaware corporation (we, us, Ultragenyx or the Company), which will be held on May 15, 2025, at 9:00 a.m. Pacific Time virtually via the Internet at *www.virtualshareholdermeeting.com/RARE2025* (Annual Meeting). Instructions on how to participate in the Annual Meeting and demonstrate proof of stock ownership are included in this proxy statement (Proxy Statement). The webcast of the Annual Meeting will be archived for one year after the date of the Annual Meeting at *www.virtualshareholdermeeting.com/RARE2025*. Only stockholders who held stock at the close of business on the record date, March 24, 2025, may vote at the Annual Meeting or any adjournment or postponement thereof.

In the event of a technical malfunction or other situation that the meeting chair determines may affect the ability of the Annual Meeting to satisfy the requirements for a meeting of stockholders to be held by means of remote communication under the Delaware General Corporation Law, or that otherwise makes it advisable to adjourn the Annual Meeting, the chair or secretary of the Annual Meeting will convene the meeting at 12:00 p.m. Pacific Time on the date specified above and at the Company's address specified above solely for the purpose of adjourning the meeting to reconvene at a date, time and physical or virtual location announced by the meeting chair. Under either of the foregoing circumstances, we will post information regarding the announcement on the Investors page of the Company's website at *https://ir.ultragenyx.com*.

At the Annual Meeting, you will be asked to consider and vote upon: (1) the election of the two Class III director nominees named in the Proxy Statement; (2) approval of our Second Amended and Restated 2023 Incentive Plan (Second A&R 2023 Plan), (3) the ratification of the selection of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2025; (4) an advisory (non-binding) resolution to approve the compensation of our named executive officers; and (5) any other business that may properly come before the Annual Meeting or any adjournment or postponement thereof. No other items of business are expected to be considered, and no other director nominees will be entertained, at the Annual Meeting.

The accompanying Proxy Statement more fully describes the details of the business to be conducted at the Annual Meeting. Proposal No. 1 relates solely to the election of the two directors nominated by the Board of Directors. After careful consideration, our Board of Directors has unanimously approved the proposals and recommends that you vote **FOR** each of the director nominees, and **FOR** each of the other proposals described in the Proxy Statement.

We are pleased to make use of the U.S. Securities and Exchange Commission (SEC) rules that allow companies to furnish proxy materials to their stockholders via the Internet. We believe the ability to deliver proxy materials electronically allows us to provide our stockholders with the information they need, while lowering the costs of delivery and reducing the environmental impact from the distribution of our Annual Meeting materials.

We look forward to speaking with you at the Annual Meeting.

Sincerely,

Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
March 28, 2025

WHETHER OR NOT YOU EXPECT TO ATTEND THE ANNUAL MEETING, PLEASE VOTE VIA THE INTERNET AS INSTRUCTED IN THE NOTICE OF INTERNET AVAILABILITY OR, IF YOU REQUESTED AND RECEIVED A PRINTED COPY OF THE PROXY MATERIALS, COMPLETE, DATE, SIGN, AND RETURN THE ENCLOSED PROXY CARD USING THE ENCLOSED RETURN ENVELOPE OR VOTING INSTRUCTION FORM PROVIDED WITH THE PRINTED PROXY MATERIALS, AS PROMPTLY AS POSSIBLE SO THAT YOUR SHARES MAY BE REPRESENTED AT THE ANNUAL MEETING. YOU MAY ALSO VOTE AT THE VIRTUAL ANNUAL MEETING.

IMPORTANT NOTICE REGARDING THE AVAILABILITY OF PROXY MATERIALS FOR THE ANNUAL MEETING OF STOCKHOLDERS TO BE HELD ON MAY 15, 2025:

The Proxy Statement and Annual Report on Form 10-K for the fiscal year ended December 31, 2024 are available at www.proxyvote.com.

VOTING METHODS

If you are an owner of record as of the record date, you may vote via any of the following methods:

INTERNET
Visit the website at:
www.proxyvote.com

TELEPHONE
If you requested and received a proxy card, call toll-free at 1-800-690-6903

MAIL
If you requested and received a proxy card, sign, date and mail the proxy card in the enclosed envelope

AT THE MEETING:
Vote at the meeting by going to:
www.
virtualshareholdermeeting.
com/RARE2025

If you are a beneficial owner of shares held through a broker, bank or other owner of record, you must follow the voting instructions you receive from the owner of record to vote your shares.

Table of Contents

Proxy Statement Overview

This overview highlights certain information contained elsewhere in this Proxy Statement and does not contain all of the information that you should consider. You should read the entire Proxy Statement carefully before voting. For more complete information regarding our business and 2024 performance, please review our 2024 Annual Report on Form 10-K as filed with the U.S. Securities and Exchange Commission (SEC) in February 2025.

Meeting and Voting Information

Meeting Date and Meeting Time	Record Date	Location
May 15, 2025 9:00 a.m. Pacific Time	March 24, 2025	Live via audio webcast at *www.virtualshareholdermeeting.com/RARE2025*

We intend to mail the Notice Regarding the Availability of Proxy Materials containing instructions on how to access this Proxy Statement and our 2024 Annual Report on Form 10-K beginning on or about March 28, 2025 to all stockholders entitled to vote at the Annual Meeting.

Proposals		Board Vote Recommendation	For More Information See Page
Proposal 1	Election of Class III Directors	**FOR** each nominee	8
Proposal 2	Approval of the Second A&R 2023 Plan	**FOR**	13
Proposal 3	Ratification of the selection of Ernst & Young LLP as our independent auditor	**FOR**	22
Proposal 4	Say on Pay	**FOR**	25

Business Highlights

2024 was a pivotal year for the Company as we expanded access and grew revenue from our four global commercial products while also advancing our six late-stage programs in serious genetic conditions. See page 37 for a summary of our achievements in 2024.

Raised and Beat
Full Year Financial Guidance

78%
growth in Crysvita® sales in Latin America and Turkey

Impact Report Highlights

At Ultragenyx, we are committed to bringing novel products to patients for the treatment of rare and ultrarare diseases, with a focus on serious, debilitating genetic diseases. Our purpose is to lead the future of rare disease medicine as we seek to treat individuals afflicted by diseases with limited or no treatment options. We recognize that their lives and well-being are dependent upon our efforts to develop new therapies. For this reason, we are passionate about developing these therapies with the utmost urgency and care. For more information about our efforts and initiatives related to patient access, innovation and responsible business practices, please see our Impact Report for fiscal 2024 (2024 Impact Report), which will be available on our website at www.ultragenyx.com under "Ultra-Committed". Website references throughout this document are provided for convenience only, and the content on the referenced websites is not incorporated by reference into this document.

See page 31 for more information about our Impact Report.

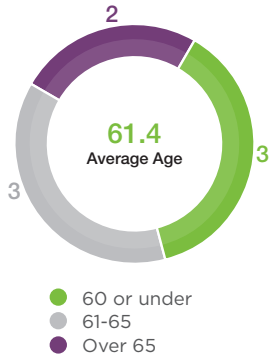
Board of Directors

The following table provides summary information about each nominee for director at the Annual Meeting and our continuing directors, as of the date of this Proxy Statement.

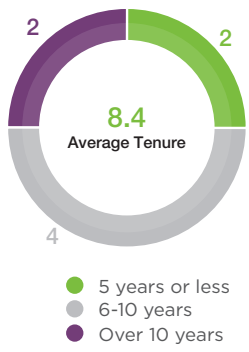
Nominee/Director Name	Age	Principal Occupation	Director Since	Year Current Term Expires	Current Director Class	Independent
Director Nominees						
Matthew K. Fust	60	Board member and advisor to various life science companies	2014	2025	III	✓
Amrit Ray, M.D.	52	Board member and advisor to various life science companies	2022	2025	III	✓
Continuing Directors						
Emil D. Kakkis, M.D., Ph.D.	64	Founder, President and CEO, Ultragenyx	2010	2026	I	✗
Shehnaaz Suliman, M.D.	53	Chief Executive Officer of ReCode Therapeutics	2019	2026	I	✓
Daniel G. Welch	67	Board member and advisor to various life science companies	2015	2026	I	✓
Deborah Dunsire, M.D.	62	Board member and advisor to various life science companies	2017	2027	II	✓
Michael Narachi	65	Board member and advisor to various life science companies	2015	2027	II	✓
Corsee D. Sanders, Ph.D.	68	Board member and advisor to various life science companies	2021	2027	II	✓

Board Composition Highlights

Age



Tenure



Building the Right Board

Our Nominating and Corporate Governance Committee is responsible for reviewing with the entire Board from time to time the appropriate skills and characteristics required of directors in the context of the current Board composition and the anticipated needs of the Board and the Company. Our Nominating and Corporate Governance Committee actively considers whether potential candidates would assist in achieving a mix of Board members that represents a broad range of knowledge, skills, and experience, including whether the nominee has specific strengths that would augment existing skills and experiences of the Board and in a manner that is aligned with the Company's strategic direction. The following matrix highlights each director's primary skills or knowledge in these areas as identified by the Nominating and Corporate Governance Committee. The matrix does not encompass all of the knowledge, skills, experiences or attributes of our directors, and the fact that a particular knowledge, skill, experience or attribute is not listed does not mean that a director does not possess it. In addition, the absence of a particular knowledge, skill, experience or attribute with respect to any of our directors does not mean the director in question is unable to contribute to the decision-making process in that area. The type and degree of knowledge, skill and experience listed below may vary among the members of the Board.

	Welch	Kakkis	Dunsire	Fust	Narachi	Ray	Sanders	Suliman
Skills and Experience								
Core Board Capabilities								
Biopharma C-level leadership	✓	✓	✓	✓	✓	✓	✓	✓
Scientific and research leadership		✓				✓	✓	✓
Clinical development leadership		✓	✓		✓	✓	✓	✓
Regulatory leadership		✓			✓	✓	✓	
Rare disease commercial experience	✓	✓	✓					
Biopharma commercial leadership	✓		✓		✓	✓		
Global access, pricing and reimbursement	✓		✓		✓	✓		
Global business operations	✓	✓	✓	✓	✓	✓	✓	✓
Finance and capital markets	✓		✓	✓	✓			✓
Corporate strategy and/or business development leadership	✓	✓	✓		✓	✓		✓
Corporate governance and board experience	✓	✓	✓	✓	✓	✓	✓	✓
Relevant / Advisory Capabilities								
Compliance (GXP, commercial)	✓	✓	✓	✓	✓	✓	✓	
Corporate legal and IP	✓		✓		✓			✓
Government affairs and policy	✓	✓	✓		✓	✓		
Human resources and organizational development	✓	✓	✓	✓	✓	✓	✓	✓
Manufacturing/supply chain	✓	✓	✓		✓			
Background								
Gender								
Male	✓	✓		✓	✓	✓		
Female			✓				✓	✓
Race/Ethnicity								
Asian						✓	✓	✓
White	✓	✓	✓	✓	✓			
LGBTQ+				✓				

Corporate Governance Overview

We are committed to maintaining good corporate governance practices and we periodically review our practices. We believe that good corporate governance, including the practices listed below, promotes the long term interests of our stockholders.

- All of our directors are independent, other than our President and Chief Executive Officer
- Director Resignation Policy that applies when a director fails to receive majority support in an uncontested election
- Completely independent Audit Committee, Nominating and Corporate Governance Committee and Compensation Committee
- Effective and active independent Chairman
- Annual Board and committee self-evaluations
- Active stockholder engagement program
- All our current directors attended 100% of the Board and committee meetings of which the director was a member in 2024
- Minimum stock ownership requirements for named executive officers and directors
- Director Overboarding Policy limiting the total number of public company boards that a director may serve to five total public company boards and public company CEO directors to three total public company boards
- Board and committees are authorized to engage outside advisors independently of management
- Clawback Policy that complies with Rule 10D-1 under the Securities Exchange Act of 1934, as amended (Exchange Act) and also includes a discretionary recoupment provision that permits recovery of all incentive compensation (including time-based and performance-based equity awards) in the event of fraud or intentional misconduct (see section entitled “Clawback Policy” of this Proxy Statement for additional details)
- Prohibition against hedging and pledging transactions by our directors and employees, including our executive officers
- Mixture of short, medium and long-tenured directors
- Corporate Governance Guidelines and robust Global Code of Conduct

PROPOSAL 1

Election of Class III Directors

Our Amended and Restated Certificate of Incorporation provides that the Board is to be divided into three classes as nearly equal in number as reasonably possible, with directors in each class generally serving three-year terms. The total Board size is currently fixed at eight directors. The Class III directors (whose terms expire at the Annual Meeting) are Matthew K. Fust and Amrit Ray, M.D. Mr. Fust and Dr. Ray were most recently elected by stockholders at the 2022 Annual Meeting. The Class I directors (whose terms expire at the 2026 Annual Meeting) are Emil D. Kakkis, M.D., Ph.D., Shehnaaz Suliman, M.D., and Daniel G. Welch. The Class II directors (whose terms expire at the 2027 Annual Meeting) are Deborah Dunsire, M.D., Michael Narachi and Corsee D. Sanders, Ph.D. The Class III directors elected at the Annual Meeting will hold office until the 2028 Annual Meeting or until their successors are elected and qualified, unless they resign or their seats become vacant due to death, removal, or other cause in accordance with our Amended and Restated Bylaws (bylaws).

As described below, the Board, upon the recommendation of the Nominating and Corporate Governance Committee, has nominated the director nominees listed above for election as directors at the Annual Meeting. They have indicated their willingness and ability to serve if elected. Should any of them become unable or, for good cause, unwilling to serve, the persons named on the enclosed proxy card as proxy holders may vote all proxies given in response to this solicitation for the election of a substitute nominee(s) chosen by the Board or the Board may reduce the size of the Board.

Nomination of Directors

The Nominating and Corporate Governance Committee reviews and recommends to the Board potential nominees for election to the Board. In reviewing potential nominees, the Nominating and Corporate Governance Committee considers the qualifications of each potential nominee in light of the Board's existing and desired mix of experience and expertise. Specifically, the Nominating and Corporate Governance Committee considers each potential nominee's personal and professional ethics, integrity, values, experience, interest in the Company, and commitment to the representation of the long-term interests of the stockholders. As described more fully above under "Proxy Statement Overview – Building the Right Board", the Nominating and Corporate Governance Committee also considers each potential nominee's contribution to the Board's composition as whole with in achieving a mix of knowledge, skills, experience, and background. The Board has adopted a policy in the Company's Corporate Governance Guidelines, which provides that as part of the search process for each new director, the Nominating and Corporate Governance Committee will add diverse candidates into the pool of candidates (and instructs any search firm the Nominating and Corporate Governance Committee engages to do so). Directors ultimately are selected based on the skills, experiences and qualifications that best support the Company in the context of the Board as a whole.

Additionally, the Nominating and Corporate Governance Committee considers whether a nominee will be able to dedicate sufficient time to, and focus on, his or her duties as a member of the Board. The Board membership criteria are set forth in our Corporate Governance Guidelines, a copy of which is available on our website at *www.ultragenyx.com* in the "Corporate Governance" subsection of the "Investors" tab. The Nominating and Corporate Governance Committee assesses its effectiveness in balancing these considerations in connection with its annual evaluation of the composition of the Board.

After reviewing the qualifications of potential Board candidates, the Nominating and Corporate Governance Committee presents its recommendations to the Board, which selects the final director nominees. We did not pay any fees to any third party to identify or assist in identifying or evaluating nominees for the Annual Meeting.

The Nominating and Corporate Governance Committee considers stockholder-recommended director nominees using the same criteria set forth above and in the same manner as director candidates recommended by other sources. Stockholders who wish to recommend a potential nominee to the Nominating and Corporate Governance Committee for consideration for election at a future annual meeting of stockholders must submit such recommendation to the Nominating and Corporate Governance Committee as described in the section entitled "Stockholder Communications" and provide the Nominating and Corporate Governance Committee with the same information that would be required to nominate a director candidate in accordance with the process and within the deadline for nominating director candidates set forth below under the question *"When are other proposals and director nominations for next year's annual meeting due?"* in the section entitled "Additional Information".

Nominees and Incumbent Directors

Information regarding our director nominees and our current directors, including their respective age as of the date of this Proxy Statement and their principal occupation, is set forth below.

Class III Directors Nominated for Election

Matthew K. Fust

Board member and advisor to various life science companies

Age: 60
Director since: 2014
INDEPENDENT
Committees: 2
Other Public Directorships: 3

Mr. Fust is a board member and advisor to life science companies. Mr. Fust currently serves on the board of directors of Atara Biotherapeutics, Inc., Crinetics Pharmaceuticals, Inc. and Neumora Therapeutics Inc., all of which are publicly traded biopharmaceutical companies. Mr. Fust also previously served on the board of directors of Dermira, Inc., a biopharmaceutical company, from August 2014 to February 2020 and the board of MacroGenics, Inc., a biotechnology company, from March 2014 to May 2020. He retired as Executive Vice President of Onyx Pharmaceuticals, Inc., a biopharmaceutical company, where he served from January 2009 to January 2014. From May 2003 to December 2008, Mr. Fust served as Chief Financial Officer at Jazz Pharmaceuticals, Inc., a specialty pharmaceutical company. From 2002 to 2003, Mr. Fust served as Chief Financial Officer at Perlegen Sciences, Inc., a biopharmaceutical company. Previously, he was Senior Vice President and Chief Financial Officer at ALZA Corporation, a pharmaceutical company, where he was an executive from 1996 to 2002. From 1991 to 1996, Mr. Fust was a manager in the healthcare strategy practice at Andersen Consulting, a consulting company. Mr. Fust holds a B.A. in Accounting from the University of Minnesota and an M.B.A. from the Stanford Graduate School of Business.

Skills and Qualifications specific to Ultragenyx:

We believe that Mr. Fust is qualified to serve on our Board due to his extensive experience in the life sciences industry, his financial experience and ability to be our "audit committee financial expert," and his service as a director of other public biopharmaceutical companies.

Amrit Ray, M.D., M.B.A.

Board member and advisor to various life science companies

Age: 52
Director since: 2022
INDEPENDENT
Committees: 1
Other Public Directorships: 1

Dr. Ray is a board member and advisor to life science companies. Dr. Ray currently serves on the board of directors of Fortrea Holdings Inc., a publicly traded, global clinical research organization, and on the board of directors of several privately owned life science companies. Previously, Dr. Ray served as Chief Patient Officer at Biohaven Ltd. a public biopharmaceutical company, from March 2022 to December 2022 when acquired by Pfizer. Prior to his role at Biohaven, he served as Senior Adviser to Bain Capital Life Sciences, an investment company, from February 2021 to March 2022. Prior to Bain Capital, Dr. Ray served as Global President, Head of R&D and Medical, for Pfizer Essential Health and subsequently the Pfizer Upjohn division at Pfizer, Inc., a public pharmaceutical company, from 2017 to January 2021. Prior to Pfizer, he held positions of increasing responsibility at Johnson & Johnson, a public pharmaceutical company, including serving as Senior Vice President, External Affairs (Science and Medicine) in 2017, Senior Vice President, Chief Medical Officer of Janssen from 2012 to 2017 and Senior Vice President, Chief Safety Officer from 2009 to 2012. Dr. Ray currently serves as a Trustee at the Board of the Hastings Center for Bioethics, and as a Visiting Professor of Practice, Faculty of Medical Sciences at Newcastle University in the United Kingdom. Dr. Ray holds a B.S., with Honours, in Immunology and a M.D. (M.B., Ch.B.) from the University of Edinburgh. He also holds an M.B.A. from the Tuck School of Business at Dartmouth College.

Skills and Qualifications specific to Ultragenyx:

We believe that Dr. Ray is qualified to serve on our Board due to his extensive experience in the life sciences industry, and particularly his research and development expertise.

Class I Directors Continuing in Office until 2026

Emil D. Kakkis, M.D., Ph.D.

Founder, President and CEO

Age: 64
Director since: 2010
NOT INDEPENDENT
Committees: 1
Other Public Directorships: 0

Dr. Kakkis is our founder and has served as our President and Chief Executive Officer and as a member of our Board since our inception in April 2010. Dr. Kakkis served as our interim principal financial officer following the departure of the Company's Chief Financial Officer in November 2022 until the appointment of Mr. Horn as the Company's Chief Financial Officer in October 2023. Prior to Ultragenyx, from September 1998 to February 2009, Dr. Kakkis served in various executive capacities, and ultimately as Chief Medical Officer, at BioMarin Pharmaceutical Inc., a biopharmaceutical company. Dr. Kakkis then served as a development consultant to BioMarin from 2009 to 2010. Dr. Kakkis is also Founder of EveryLife Foundation for Rare Diseases, a non-profit organization he started in 2009 to accelerate biotechnology innovation for rare diseases. Dr. Kakkis received the Termeer Visionary Leadership Award in 2019 and the Leadership Award from the California Life Sciences Association in 2021. Dr. Kakkis is board certified in Medical Genetics and was board certified in Pediatrics. He holds a B.A. in Biology from Pomona College and combined M.D. and Ph.D. degrees from the UCLA School of Medicine's Medical Scientist Training Program where he received the Bogen prize for his research.

Skills and Qualifications specific to Ultragenyx:

We believe that Dr. Kakkis possesses specific expert knowledge of genetics and rare diseases and operational experience in the life sciences sector that qualify him to serve on our Board.

Shehnaaz Suliman, M.D., M.Phil., M.B.A

Chief Executive Officer of ReCode Therapeutics

Age: 53
Director since: 2019
INDEPENDENT
Committees: 2
Other Public Directorships: 1

Dr. Suliman has served as Chief Executive Officer of ReCode Therapeutics, a privately-held, integrated genetic medicines company, since January 2022. Prior to joining ReCode Therapeutics, Dr. Suliman served as President and Chief Operating Officer of Alector, Inc., a clinical stage biotechnology company, from December 2019 to December 2021 and previously served as Senior Vice President, Corporate Development and Strategy of Theravance Biopharma, Inc., a biopharmaceutical company, from July 2017 to March 2019. Prior to her position at Theravance, Dr. Suliman worked for Genentech, Inc., a biopharmaceutical company, as Group Leader and Project Team Leader in the R&D Portfolio Management and Operations Group from September 2010 to May 2015 and then as Vice President and Global Therapeutic Head, Roche Partnering from June 2015 to July 2017. Prior to Genentech, Dr. Suliman held various management roles of increasing responsibility at Gilead Sciences, Inc., a biopharmaceutical company, from January 2005 and September 2010. Prior to Gilead, Dr. Suliman was an investment banker with Lehman Brothers and Petkevich & Partners, advising public and private companies on buy- and sell-side transactions. She is a member of the board of directors of 10X Genomics, Inc., a publicly traded life science technology company. Dr. Suliman received her M.D. at the University of Cape Town Medical School, South Africa, and holds an M.B.A, with distinction, and M.Phil. in Development Studies from Oxford University, where she was a Rhodes Scholar.

Skills and Qualifications specific to Ultragenyx:

We believe that Dr. Suliman is qualified to serve on our Board due to her extensive operational experience with global biopharmaceutical companies, and particularly her expertise in business development, corporate strategy and clinical drug development.

Daniel G. Welch

Board member and advisor to various life science companies

Age: 67
Director since: 2015
INDEPENDENT CHAIRMAN
Committees: 2
Other Public Directorships: 2

Mr. Welch is a board member and advisor to life science companies. Mr. Welch currently serves as chairman on the boards of Structure Therapeutics, Inc. and Prothena Corporation plc, each a publicly traded biotechnology company. Between January 2015 and January 2018, he was an Executive Partner at Sofinnova Ventures, a venture capital firm. Prior to Sofinnova, Mr. Welch served as Chairman, Chief Executive Officer, and President of InterMune, Inc., a biotechnology company, from May 2008 to October 2014 and served as President and Chief Executive Officer of InterMune and a member of its board of directors from September 2003 to May 2008. From August 2002 to January 2003, Mr. Welch served as Chairman and Chief Executive Officer of Triangle Pharmaceuticals, Inc., a pharmaceutical company. From October 2000 to June 2002, Mr. Welch served as President of the pharmaceutical division of Elan Corporation, plc. Mr. Welch previously served as chairman of the board of directors of Nuvation Bio from July 2020 to September 2024 and as a director on the boards of directors of Intercept Pharmaceuticals, Inc from November 2015 to June 2021 and Seagan Inc. from July 2007 to December 2023. Mr. Welch holds a B.S. from the University of Miami and an M.B.A. from the University of North Carolina.

Skills and Qualifications specific to Ultragenyx:

We believe that Mr. Welch is a strong operating executive with operational and strategic expertise in the global pharmaceutical market, whose experience contributes valuable insight to the Board.

Class II Directors Continuing in Office until 2027

Deborah Dunsire, M.D.

Board member and advisor to various life science companies

Age: 62
Director since: 2017
INDEPENDENT
Committees: 2
Other Public Directorships: 1

Dr. Dunsire is a board member and advisor to life science companies. Dr. Dunsire served as President and Chief Executive Officer of H. Lundbeck A/S, a pharmaceutical company, from September 2018 until August 2023. She previously served as President and Chief Executive Officer and as a director of Xtuit Pharmaceuticals, Inc., a private biopharmaceutical company, from January 2017 to March 2018. Prior to her position at Xtuit, she served as President and Chief Executive Officer and a director of FORUM Pharmaceuticals Inc., a private pharmaceutical company, from July 2013 to May 2016. Prior to FORUM, Dr. Dunsire worked for Takeda Pharmaceutical Company Limited, a publicly traded pharmaceutical company, as a corporate officer from June 2010 to June 2011 and a director from June 2011 to June 2013. She served as President and Chief Executive Officer and as a director of Millennium Pharmaceuticals, Inc., a publicly traded biopharmaceutical company, between 2005 and 2008, when it was acquired by Takeda, and then as President and Chief Executive Officer of Millennium: The Takeda Oncology Company after the acquisition between 2008 and 2013. Prior to Millennium, Dr. Dunsire held various roles of increasing responsibility at Novartis Pharma AG between 1988 and 2005. Dr. Dunsire currently serves on the board of McKesson Corporation, a publicly traded healthcare services company. She previously served on the board of directors of Syros Pharmaceuticals, a publicly traded biotech company, from September 2021 to November 2024 and of Alexion Pharmaceuticals Inc., a publicly traded biotech company, from January 2018 until July 2021 when it was acquired by AstraZeneca. She obtained an MBBCh from the University of the Witwatersrand.

Skills and Qualifications specific to Ultragenyx:

We believe that Dr. Dunsire is qualified to serve on our Board due to her extensive experience in the biotechnology and pharmaceutical sectors, including service as the chief executive officer of various pharmaceutical companies, which gives her the skills to provide us with operational and strategic insights.

Michael Narachi

Board member and advisor to various life science companies

Age: 65
Director since: 2015
INDEPENDENT
Committees: 2
Other Public Directorships: 0

Mr. Narachi previously served as President and Chief Executive Officer of CODA Biotherapeutics, Inc., a private biotherapeutics company, from August 2018 through October 2022 and served as a director of CODA Biotherapeutics until the company's sale in March 2023. Between March 2009 and July 2018, Mr. Narachi served as President, Chief Executive Officer and director of Orexigen Therapeutics, Inc., a biotechnology company. Orexigen filed for reorganization under Chapter 11 of the U.S. Bankruptcy Code in March 2018. Previously, Mr. Narachi served as Chairman, Chief Executive Officer, and President of Ren Pharmaceuticals, Inc., a private biotechnology company, from November 2006 to March 2009. In 2004, Mr. Narachi retired as Vice President of Amgen Inc., a leading therapeutics company, where he served as General Manager of Amgen's Anemia Business from 1999 to 2003, until his retirement in 2004. Mr. Narachi joined Amgen in 1984 and held various senior positions throughout the organization over a 20-year career including global development leader for Neupogen/Neulasta, Vice President of development and representative director for Amgen Japan; head of corporate strategic planning; Chief Operations Officer of Amgen Colorado; and vice president, licensing and business development. Mr. Narachi previously served on the board of directors of BIO, the Biotechnology Innovation Organization, as a member of the board of directors of PhRMA, the Pharmaceutical Research and Manufacturers of America, and as the chairman of the board of directors of Celladon Corporation, a publicly traded gene therapy company, from October 2013 to March 2016, and as a director of AMAG Pharmaceuticals, Inc., a publicly traded specialty pharmaceutical company, from November 2006 to April 2014. Mr. Narachi holds a B.S. in Biology and an M.A. in Biology and Genetics from the University of California, Davis. He also holds an M.B.A. from the Anderson Graduate School of Management at the University of California, Los Angeles.

Skills and Qualifications specific to Ultragenyx:

We believe that Mr. Narachi is qualified to serve on our Board due to his extensive experience in the life sciences industry, his service as the chief executive officer of various biotechnology companies, and his membership on various boards of directors in the biotechnology and pharmaceutical sectors, all of which give him the skills to provide us with operational and strategic insights.

Corsee D. Sanders, Ph.D.

Board member and adviser to various life science companies

Age: 68
Director since: 2021
INDEPENDENT
Committees: 2
Other Public Directorships: 3

Dr. Sanders is a board member and advisor to life science companies. Dr. Sanders currently serves as a member of the board of directors of Beigene Ltd., Molecular Templates Inc. and Legend Biotech Corporation, each a publicly traded biotechnology company. She currently serves as a co-chair of the Board of Advisors, and Chair of the Science and Technology Advisory Committee for the Fred Hutchinson Cancer Center. She most recently served as Executive Vice President at Juno Therapeutics, Inc., a biopharmaceutical company, from 2017 to 2018 and strategic advisor to the Chief Medical Officer of Celgene Corporation, a biopharmaceutical company, from 2018 to 2019 following Juno's acquisition by Celgene. Following the acquisition of Celgene by Bristol Myers Squibb, Dr. Sanders served as Transition Advisor to the Clinical Development team at BMS from 2019 to 2020. Prior to her role at BMS, she held positions of increasing responsibility at Genentech/Roche, a biotechnology company, from 1994 to 2017, including serving as Senior Vice President, Global Head of Clinical Operations and Industry Collaboration, from 2012 to 2017. Dr. Sanders holds a B.S. and M.S. in Statistics, *magna cum laude*, from the University of the Philippines. She also holds an M.A. and Ph.D. in Statistics from the Wharton Doctoral Program at the University of Pennsylvania.

Skills and Qualifications specific to Ultragenyx:

We believe that Dr. Sanders is qualified to serve on our Board due to her established and extensive experience in global clinical development and her role as an advisor and director to various companies in the biotechnology and pharmaceutical sectors, all of which give her the skills to provide us with operational and strategic insights.

Vote Required

The two nominees who receive the greatest number of affirmative votes will be elected as Class III directors. Shares as to which a stockholder withholds voting authority and broker non-votes, if any, are not considered votes cast and therefore will have no effect on the vote outcome.

Director Resignation Policy

We have a Director Resignation Policy, which is set forth in our Corporate Governance Guidelines, a copy of which is available on our website in the "Corporate Governance" subsection of the "Investors" tab. The policy establishes that any director nominee who receives more "withhold" votes than "for" votes in an uncontested election of directors is expected to tender his or her resignation promptly following the certification of the election results. Broker non-votes, if any, are not counted as either a "withhold" or "for" vote.

The Nominating and Corporate Governance Committee will promptly consider the tendered resignation and make a recommendation to the Board. The Board will act on the recommendation of the Nominating and Corporate Governance Committee no later than 90 days following the certification of the election results. The Board will promptly and publicly disclose its decision and, if applicable, the reasons for rejecting the tendered resignation.

THE BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" EACH OF THE DIRECTOR NOMINEES IDENTIFIED ABOVE.

PROPOSAL 2

Approval of the Ultragenyx Pharmaceutical Inc. Second Amended and Restated 2023 Incentive Plan

On March 24, 2025, the Board approved a second amendment and restatement of the Ultragenyx Pharmaceutical Inc. 2023 Incentive Plan (the 2023 Plan and as amended and restated, the Second A&R 2023 Plan), subject to stockholder approval at the Annual Meeting. The Second A&R 2023 Plan provides for an additional 3.0 million shares of our common stock to be available for issuance thereunder and extends the term of the plan through May 15, 2035. We believe that our equity compensation policies enable us to attract and retain a highly-skilled team of executives and aligns our executives' interests with those of our stockholders by rewarding short-term and long-term performance and tying compensation to increases in stockholder value. If the Second A&R 2023 Plan is approved by our stockholders, we intend to file a Form S-8 with the SEC following the Annual Meeting during the second or third quarter that covers the additional shares reserved for issuance under the Second A&R 2023 Plan.

Share Reserve Under the Second A&R 2023 Plan

The maximum number of shares of our common stock authorized for issuance under the Second A&R 2023 Plan is (i) 11.5 million shares plus (ii) the number of shares subject to any award outstanding under the 2014 Incentive Plan (2014 Plan) or the 2011 Incentive Plan (2011 Plan and together with the 2014 Plan, the Prior Plans) as of June 7, 2023 that after June 7, 2023 are not issued because such award is forfeited, canceled, terminates, expires or otherwise lapses without being exercised, or is settled in cash. Based on the recent range of our stock price, our current compensation practices, our anticipated future awards, as well as our three-year burn rate, we believe the Second A&R 2023 Plan share reserve will be sufficient for us to grant equity awards for approximately one year based on our stock price and compensation philosophy and policies. If stockholders do not approve this Proposal No. 2, we anticipate that the shares that remain available for grant would be insufficient for us to continue to provide equity incentives at a competitive market level, limiting our ability to attract and retain talented employees and other service providers, and requiring a greater cash allocation to support our incentive programs.

As part of the Compensation Committee's recommendation to the Board to approve the Second A&R 2023 Plan and the additional shares available for issuance under the Second A&R 2023 Plan, the Compensation Committee considered advice from Aon, its independent compensation consultant. The Compensation Committee also carefully analyzed our historical burn rate, anticipated future equity award needs to help drive our long-term strategic plan, and the dilutive impact of the Second A&R 2023 Plan's share reserve.

Reasons for Seeking Stockholder Approval

We believe the following are important considerations for stockholders in determining whether to approve the Second A&R 2023 Plan:

- **Equity Awards are Essential to Talent Acquisition and Retention:** Equity awards, similar to those typically offered by our competitors are, and we believe will continue to be, an integral component of our overall compensation program, enabling us to attract qualified and skilled employees and directors, retain our existing employees, including our experienced management team, and provide incentives for our employees to exert maximum efforts for our success, ultimately contributing to the creation of stockholder value. If the Second A&R 2023 Plan is not approved by our stockholders at the Annual Meeting, we will not have adequate shares to continue to grant equity awards to all our employees and directors in 2025. Historically, we have granted equity awards deeply in our organization, believing that a culture of ownership is important to our ability to achieve our short- and long-term business objectives and that our success is dependent on our employees feeling invested in our future. In fiscal 2024, we granted equity awards to 1,376 employees.
- **We are Committed to Executing on our Strategic Priorities:** The use of equity awards assists us and will continue to assist us in ensuring that our executives and employees are focused on long term value creation for our stockholders and in enabling us to attract and retain the talent needed to execute on our strategic priorities while managing our cash flow. We believe that the approval of the Second A&R 2023 Plan as described in this proposal is instrumental to our ongoing success and our ability to provide increased value to our stockholders.
- **We are Managing our Annual Burn Rate:** We carefully and thoughtfully manage our equity award use, balancing attraction, retention and incentivization of our employees against dilution and burn rate considerations. We have relied more heavily on the grant of restricted stock units (RSUs) and for our executives, performance stock units (PSUs) as opposed to options in an effort to manage our burn rate. Further, we regularly review and consider our burn rate against those of our peer companies in the biotech industry to provide incentives at a competitive market level as part of our human capital management strategy.

- **Our Equity Program is Performance-Based:** The Compensation Committee believes that PSUs align the objectives of management with those of our stockholders with respect to long-term performance and success of the Company. For 2024, the equity grants to our executive officers, other than to our Chief Executive Officer, reflected an equal value split among option, RSUs and PSUs. To further align the compensation of our executive officers with stockholder interests and to increase the portion of compensation tied to Company performance measures, the Compensation Committee made the following changes:
  - In 2024, the Compensation Committee changed the equity award value split for our Chief Executive Officer from an equal value split among options, RSUs and PSUs to 20% options, 20% RSUs and 60% PSUs;
  - In 2025, the Compensation Committee increased the portion of PSUs for our other executive officers from 25% to 50% resulting in an awards split of 25% RSUs, 25% options and 50% PSUs.
- **Forecasted Usage.** If stockholders approve the Second A&R 2023 Plan, the Compensation Committee currently anticipates that we will likely need to again request additional shares at our 2026 Annual Meeting of Stockholders, based on our current share price, recent burn rate history, and historical new hire and annual grant practices. In making this determination, the Compensation Committee took into account the potential impact of any expected future changes in employee population on projected share use, in particular given our ongoing efforts to execute on our strategic priorities. We cannot predict our future equity grant practices, the future price of our shares or future hiring activity with any degree of certainty at this time, and the share reserve under the Second A&R 2023 Plan could last for a shorter or longer time.

Key Features and Governance Best Practices

The Second A&R 2023 Plan reflects a number of provisions that protect stockholders and reflect corporate governance best practices, including the following:

- **No Repricing and No Reload Options:** Without stockholder approval, the Second A&R 2023 Plan prohibits the repricing of stock options and SARs (defined below), the exchange or substitution of one award for another award that has the effect of reducing the exercise or purchase price, and the cancellation or exchange of underwater awards for cash, another award or other property, except in the event of a change in our capitalization or a covered transaction (described below). Reload options are not permitted under the Second A&R 2023 Plan.
- **No Dividends on Unvested Awards:** The Second A&R 2023 Plan provides that dividends and dividend equivalent rights may never be paid on any unvested award.
- **No Liberal Share Recycling:** The Second A&R 2023 Plan prohibits liberal share recycling.
- **Limit on Non-Employee Director Compensation:** The Second A&R 2023 Plan contains an annual limit on cash and equity-based compensation that may be paid or granted, whether under the Second A&R 2023 Plan or otherwise, to our non-employee directors of $900,000 (or $1,500,000 in the calendar year that the non-employee director first joins the Board or if the non-employee director is serving as chairman or lead director of the Board).
- **Clawback Provision:** Awards under the Second A&R 2023 Plan are subject to our clawback policy. In addition, the Plan Administrator (as defined below) may cancel or limit awards under the Second A&R 2023 Plan if a participant is not in compliance with the applicable award agreement or if a participant breaches any confidentiality agreement with the Company.
- **No Automatic Single Trigger Acceleration:** In the event of a covered transaction, the Second A&R 2023 Plan does not provide for automatic single trigger acceleration.
- **Term and Exercise Price Limits on Options and SARs:** Options and SARs granted under the Second A&R 2023 Plan are subject to a maximum term of 10 years and may not be granted at a discount to the fair market value of our common stock on the grant date.
- **No Tax Gross-Ups.** The Second A&R 2023 Plan does not provide for any tax gross-ups.
- **No Evergreen:** There is no automatic share reload or "evergreen" provision in the Second A&R 2023 Plan.

Shares Remaining Under the Prior Plans

As of March 7, 2025, a total of 93,892,528 shares of our common stock were outstanding and the fair market value of our common stock was $38.62 based on the closing sale price of our common stock on the Nasdaq Global Select Market as of that date. The following table sets forth information regarding outstanding equity awards and shares available for future equity awards under the 2023 Plan (without giving effect to approval of the Second A&R 2023 Plan), the Prior Plans, our Employment Inducement Plan, as amended (the "Inducement Plan), the Dimension Therapeutics, Inc. 2015 Stock Option and Incentive Plan (the "DT 2015 Plan), the Dimension Therapeutics, Inc. 2013 Stock Plan (the "DT 2013 Plan"), and the shares available for future equity awards under our Amended and Restated 2014 Employee Stock Purchase Plan (ESPP) as of March 7, 2025.

	2023 Plan	2014 Plan	2011 Plan	DT 2015 Plan	DT 2013 Plan	Inducement Plan	Aggregate Under All Plans
Total shares underlying outstanding stock options	2,399,511	8,459,896	—	21,403	221	268,183	11,149,214
Weighted average exercise price of outstanding stock options	48.43	68.50	—	49.33	31.78	46.88	63.62
Weighted average remaining life of outstanding stock options	9.4	4.8	—	1.1	0.2	7.7	5.9
Total shares underlying outstanding RSUs	4,301,616	1,265,530	—	—	—	587,676	6,154,822
Total shares underlying outstanding PSUs (assuming target performance)	619,640	115,318	—	—	—	—	734,958
Total shares available for issuance (assuming outstanding PSUs vest at maximum performance)	2,493,498	—	—	—	—	200,413	2,693,911

Dilution

Dilution is commonly measured by "overhang," which generally refers to the total number of equity awards outstanding plus the total number of shares available for grant under our equity plans, divided by the sum of the total common stock outstanding, the number of equity awards outstanding and the total number of shares available for grant under our equity plans. If the Second A&R 2023 Plan is approved, our overhang will be approximately 21% as of March 7, 2025; however, many of the stock options attributing to our overhang are underwater.

As shown above, we had approximately 11,149,214 stock options outstanding, with a weighted average exercise price of $63.62 as of March 7, 2025. That included 7,727,822 options currently exercisable, with a weighted average exercise price of $70.07, and 3,421,392 options not yet vested, with a weighted average exercise price of $49.05. That compares to a closing stock price on March 7, 2025, of $38.62. The 7,638,237 stock options currently underwater account for 6% of our overhang if the Second A&R 2023 Plan is approved.

Historical Burn Rate

Our equity plan share usage over 2022, 2023 and 2024 represented a three-year average burn rate of 5.75%, as described in the table below.

Year	Weighted Average Common Stock Outstanding	Time-based Stock Options Granted	Performance-based Stock Options Granted	Performance-based Stock Options Earned	RSUs Granted	PSUs Granted	PSUs Earned	Annualized Burn Rate[(1)]
2022	69,914,225	2,293,950	1,827,449	0	1,347,125	166,730	28,990	5.25%
2023	73,543,862	2,123,256	0	152,593	2,447,170	362,470	27,581	6.46%
2024	90,538,118	1,445,364	0	342,622	3,169,688	274,484	47,464	5.53%
Three-Year Average								**5.75%**

(1) Annualized burn rate defined as: time-based stock options granted, performance-based stock options earned, RSUs granted and PSUs earned as a percentage of weighted average common shares outstanding.

Summary of the Second A&R 2023 Plan

The following summary describes the material terms of the Second A&R 2023 Plan. This summary of the Second A&R 2023 Plan is not a complete description of all provisions of the Second A&R 2023 Plan and is qualified in its entirety by reference to the Second A&R 2023 Plan, which is attached hereto as Appendix A. Stockholders are encouraged to read the Second A&R 2023 Plan in its entirety.

Purpose

The purpose of the Second A&R 2023 Plan is to advance the Company's interests by providing for the grant to participants of equity and other incentive awards.

Plan Administration

The Compensation Committee serves as the primary administrator of the Second A&R 2023 Plan, except that the Compensation Committee may, subject to applicable law, delegate authority to one or more members of the Board or one or more of our officers or employees (the Compensation Committee or such delegee, the Plan Administrator).

The Plan Administrator has the authority to, among other things, (i) interpret and construe the Second A&R 2023 Plan, any rules and regulations under the Second A&R 2023 Plan and the terms and conditions of any award granted under the Second A&R 2023 Plan, (ii) determine eligibility for and grant awards under the Second A&R 2023 Plan, (iii) determine, modify or waive the terms and conditions of awards under the Second A&R 2023 Plan, (iv) prescribe forms, rules and procedures relating to the Second A&R 2023 Plan, (v) establish and verify the extent of satisfaction of any performance goals or other conditions applicable to the grant, issuance, retention, vesting, exercisability or settlement of any award under the Second A&R 2023 Plan, and (vi) otherwise do all things necessary or appropriate to carry out the purposes of the Second A&R 2023 Plan. The Plan Administrator's determinations under the Second A&R 2023 Plan are conclusive and binding.

Authorized Shares

Subject to adjustment as described below, the maximum number of shares of our common stock that may be delivered in satisfaction of awards under the Second A&R 2023 Plan is (i) 11.5 million, plus (ii) the number of shares of common stock subject to any award under a Prior Plan as of June 7, 2023 that become available as a result of the termination, cancellation or forfeiture of such awards under such Prior Plan after June 7, 2023.

Shares of our common stock to be issued under the Second A&R 2023 Plan may be authorized but unissued shares of our common stock or previously issued shares acquired by us. If any shares of our common stock underlying awards that are settled in cash, canceled, forfeited or otherwise expire or lapse without being exercised (to the extent applicable), the shares of common stock allocable to the terminated portion of such award will again be available for issuance under the Second A&R 2023 Plan.

However, notwithstanding the foregoing, the following shares of common stock will not be available for issuance under the Plan: (a) shares withheld from an award under the Second A&R 2023 Plan or a Prior Plan to satisfy the tax withholding obligations with respect to such award, (b) shares withheld from an award under the Second A&R 2023 Plan or a Prior Plan in payment of the exercise price of an award requiring exercise, (c) shares repurchased on the open market by us using proceeds from the exercise price paid with respect to awards under the Second A&R 2023 Plan or a Prior Plan, or (d) gross shares subject to an SAR granted under the Second A&R 2023 Plan or a Prior Plan that are not issued in connection with the stock-settlement of such SAR.

Limits on Non-Employee Director Compensation

The aggregate dollar value of equity-based (based on the grant date fair value of equity-based awards determined for financial reporting purposes) and cash compensation granted under the Second A&R 2023 Plan or otherwise to any one non-employee director during any fiscal year will not exceed $900,000, with up to $1,500,000 to be permitted for a non-employee director in the fiscal year he or she first joins our Board or is first designated as Chairman of our Board or Lead Director.

Eligibility

The Plan Administrator will select participants from among our, and our affiliates', executives, employees in good performance standing, directors, consultants and advisors who are in a position to contribute significantly to our success and the success of our affiliates. Eligibility for options intended to be incentive stock options, or ISOs, is limited to our employees or the employees of certain of our affiliates. As of March 7, 2025, there were approximately 1,279 employees (including eight executive officers) and seven non-employee directors who would be eligible to participate in the Second A&R 2023 Plan. As of March 7, 2025, no consultants or advisors would be eligible to participate in the Second A&R 2023 Plan.

Awards Under the Second A&R 2023 Plan

The Second A&R 2023 Plan provides for grants of stock options, SARs, restricted and unrestricted stock, stock units (including RSUs), performance awards, cash awards and other awards convertible into or otherwise based on shares of our common stock. Dividend equivalents may also be provided in connection with an award under the Second A&R 2023 Plan (other than stock options and SARs), provided that such dividend equivalents will be subject to the same limits or restrictions as the awards to which they relate, and will not be payable until such awards vest.

Stock Options

A stock option is an award that entitles the participant to receive, upon exercise, shares of our common stock upon payment of the exercise price. The exercise price of an option may not be less than the fair market value (or, in the case of an ISO granted to a ten percent shareholder, 110% of the fair market value) of a share of our common stock on the date of grant. The Plan Administrator will determine the time or times at which stock options become exercisable and the terms on which they remain exercisable. The maximum term of a stock option is 10 years (or, in the case of an ISO granted to a ten percent shareholder, five years). Reload stock options are prohibited under the Second A&R 2023 Plan.

SARs

SARs entitle the participant to receive, upon exercise, shares of our common stock or cash equal to the excess of the value of the shares subject to the SAR over the exercise price. The exercise price of an SAR may not be less than the fair market value of a share of our common stock on the date of grant. The Plan Administrator will determine the time or times at which SARs become exercisable and the terms on which they remain exercisable. The maximum term of an SAR is 10 years.

Restricted and Unrestricted Stock

A restricted stock award is an award of our common stock subject to restrictions requiring that it be redelivered or offered for sale to the Company if specified conditions are not satisfied, while an unrestricted stock award is an award of our common stock that is not subject to any restrictions. The Plan Administrator will determine the terms of awards of restricted and unrestricted stock.

Stock Units

A stock unit award is denominated in shares of our common stock and entitles the participant to receive stock or cash measured by the value of the shares in the future. An RSU is a stock unit award that is subject to the satisfaction of performance conditions or other vesting conditions. The Plan Administrator will determine the terms of awards of stock units, including RSUs.

Performance Awards

A performance award is an award under the Second A&R 2023 Plan where the vesting, settlement or exercisability is subject to specified performance criteria.

Cash Awards

Cash awards are awards under the Second A&R 2023 Plan that are denominated in cash.

Termination of Employment

The Plan Administrator will determine the effect of termination of employment or service on an award under the Second A&R 2023 Plan. Unless otherwise expressly provided by the Plan Administrator, upon a termination of a participant's employment all unvested options then held by the participant and other awards requiring exercise will terminate and all other unvested awards will be forfeited and all vested stock options and SARs then held by the participant will remain outstanding for three months, or one year in the case of death, or, in each case, until the applicable expiration date, if earlier. All stock options and SARs held by a participant immediately prior to the participant's termination of employment will immediately terminate upon termination of employment if the termination is for cause or occurs in circumstances that, in the determination of the Plan Administrator, would have constituted grounds for the participant's employment to be terminated for cause.

Transferability

Awards under the Second A&R 2023 Plan may not be transferred except by will or by the laws of descent and distribution. For awards other than ISOs, the Plan Administrator may permit the transfer not for value to any transferee eligible to be covered by the provisions of Form S-8.

Clawback; Recovery of Compensation

Awards granted under the Second A&R 2023 Plan are subject to forfeiture, termination and rescission, and a participant will be obligated to return to us the value received with respect to awards, to the extent provided by the Plan Administrator in an award agreement, pursuant to Company policy relating to the recovery of erroneously-paid incentive compensation (including our Clawback Policy), or as otherwise required by law or applicable stock exchange listing standards.

Covered Transaction

In the event of a covered transaction (as defined in the Second A&R 2023 Plan), the Plan Administrator may, among other things, provide for (i) continuation or assumption of outstanding awards, (ii) new grants in substitution of outstanding awards, (iii) the accelerated vesting or delivery of shares under awards or for a cash-out of outstanding awards, in each case on such terms and with such restrictions as it deems appropriate. However, if the award is not continued or assumed or a new grant is not substituted for the award, then stock options and SARs will become fully exercisable and all other awards shall become vested (with any performance based on target or actual performance as determined by the Plan Administrator).

Prohibition Against Repricing

We will not, without stockholder approval (except in the case of a change in our capitalization, as described below), (i) reduce the exercise price of a stock option or SAR, (ii) other than in the case of covered transaction, at any time when the exercise price of a stock option or SAR is above the fair market value of a share of stock, cancel and re-grant or exchange such stock option or SAR for cash or a new award having a lower (or no) exercise price, or (iii) take any other action with respect to an award that would be treated as a repricing under generally accepted accounting principles.

Adjustment

In the event of a stock dividend, stock split or combination of shares including a reverse stock split, recapitalization or other change in our capital structure that constitutes an equity restructuring within the meaning of the Financial Accounting Standards Board, Accounting Standards Codification Topic 718, *Compensation — Stock Compensation,* the Plan Administrator will make appropriate adjustments to the maximum number of shares that may be delivered under the Second A&R 2023 Plan, and will also make appropriate adjustments to the number and kind of shares of stock or securities subject to awards, the exercise prices of such awards or any other terms of awards affected by such change. The Plan Administrator will also make the types of adjustments described above to take into account distributions and other events other than those listed above if it determines that such adjustments are appropriate to avoid distortion and preserve the value of awards.

Amendment and Termination

The Plan Administrator will be able to amend the Second A&R 2023 Plan or outstanding awards for any purpose which may at the time be permitted by law, or terminate the Second A&R 2023 Plan as to future grants of awards, except that the Plan Administrator will not be able to alter the terms of an award if it would affect materially and adversely a participant's rights under the award without the participant's consent (unless expressly provided in the Second A&R 2023 Plan or the right to alter the terms of an award was expressly reserved by the Plan Administrator at the time the award was granted). Stockholder approval will be required for any amendment to the Second A&R 2023 Plan to the extent such approval is required by law, including the Internal Revenue Code of 1986, as amended (the "Code"), or applicable stock exchange requirements. No awards may be made under the Second A&R 2023 Plan after 10 years from June 7, 2023.

New Plan Benefits

As described above, the selection of participants who will receive awards under the Second A&R 2023 Plan and the size and types of awards will be determined by the Plan Administrator in its discretion. Therefore, the amount of any future awards under the Second A&R 2023 Plan is not yet determinable and it is not possible to predict the benefits or amounts that will be received by, or allocated to, particular individuals or groups of employees.

Awards Granted Under the 2023 Plan

No awards granted under the 2023 Plan prior to the date of the Annual Meeting were subject to stockholder approval of the Second A&R 2023 Plan. Pursuant to the SEC rules, the following table sets forth information with respect to awards that have been granted under the 2023 Plan to the groups named below as of March 7, 2025, with PSUs based on achievement of target performance. No associate of any director, executive officer or director nominee has received awards under the 2023 Plan, and no person has received more than 5% of all awards under the 2023 Plan.

Name and Position	Stock Options Granted	RSUs and PSUs Granted
Emil D. Kakkis, M.D., Ph.D., President and Chief Executive Officer	148,542	326,783
Howard Horn, Chief Financial Officer and Executive Vice President, Corporate Strategy	62,360	85,760
Erik Harris, Chief Commercial Officer and Executive Vice President	64,446	89,240
Eric Crombez, M.D., Chief Medical Officer and Executive Vice President	64,446	89,240
John R. Pinion II, Chief Quality Officer and Executive Vice President, Translational Sciences	57,474	79,082
All current executive officers as a group (8)	543,616	863,869
All current directors who are not executive officers as a group (7)	69,300	37,415
Matthew K. Fust	9,900	5,345
Amrit Ray, M.D.	9,900	5,345
All current employees, including all current officers who are not executive officers, as a group (1,221)	1,899,221	4,893,071

U.S. Federal Income Tax Consequences

The following is a summary of the U.S. federal income tax treatment applicable to us and the participants who receive awards under the Second A&R 2023 Plan based on the federal income tax laws in effect on the date of this Proxy Statement. This summary is not intended to be exhaustive and does not address all matters relevant to a particular participant based on their specific circumstances. The summary expressly does not discuss the income tax laws of any state, municipality, or non-U.S. taxing jurisdiction, or the gift, estate, excise (including the rules applicable to deferred compensation under Section 409A of the Code), or other tax laws other than U.S. federal income tax law. Because individual circumstances may vary, we recommend that all participants consult their own tax advisor concerning the tax implications of awards granted under the Second A&R 2023 Plan.

Stock Option Grants

Stock options granted under the Second A&R 2023 Plan may be either ISOs, which satisfy the requirements of Section 422 of the Code, or non-statutory stock options (NSOs), which are not intended to meet such requirements. The U.S. federal income tax treatment for the two types of options differs as follows:

Incentive Stock Options

No taxable income is recognized by the participant at the time of the grant of an ISO, and no taxable income is recognized for ordinary income tax purposes at the time the ISO is exercised, although taxable income may arise at that time for alternative minimum tax purposes. Unless there is a disqualifying disposition, as described below, the participant will recognize long-term capital gain in an amount equal to the excess of (i) the amount realized upon the sale or other disposition of the purchased shares over (ii) the exercise price paid for the shares.

A disqualifying disposition occurs if the disposition is less than two years after the date of grant or less than one year after the exercise date. If there is a disqualifying disposition of the shares, then the excess of (i) the fair market value of those shares on the exercise date or (if less) the amount realized upon such sale or disposition over (ii) the exercise price paid for the shares will be taxable as ordinary income to the participant. Any additional gain or loss recognized upon the disposition will be a capital gain or loss.

If the participant makes a disqualifying disposition of the purchased shares, then we will be entitled to an income tax deduction, for the taxable year in which such disposition occurs, equal to the amount of ordinary income recognized by the participant as a result of the disposition. We will not be entitled to any income tax deduction if the participant makes a qualifying disposition of the shares.

Non-Statutory Stock Options

No taxable income is recognized by a participant upon the grant of an NSO. The participant in general will recognize ordinary income, in the year in which the NSO is exercised, equal to the excess of the fair market value of the purchased shares on the exercise date over the exercise price paid for the shares, and the participant will be required to satisfy the tax withholding requirements applicable to such income. We will be entitled to an income tax deduction equal to the amount of ordinary income recognized by the participant with respect to the exercised NSO.

SARs

No taxable income is recognized upon receipt of an SAR. The holder will recognize ordinary income in the year in which the SAR is exercised, in an amount equal to the excess of (i) the fair market value of the underlying shares of common stock on the exercise date over (ii) the base price in effect for the exercised right, and the holder will be required to satisfy the tax withholding requirements applicable to such income. We will be entitled to an income tax deduction equal to the amount of ordinary income recognized by the holder in connection with the exercise of the SAR.

Stock Awards

Participants will recognize ordinary income at the time unrestricted stock awards are granted in an amount equal to the excess of (i) the fair market value of the shares on the grant date over (ii) the cash consideration (if any) paid for the shares. The holder will be required to satisfy the tax withholding requirements applicable to the income.

No taxable income is recognized at the time restricted stock awards are issued, but the participant will have to report as ordinary income, as and when those shares subsequently vest, an amount equal to the excess of (i) the fair market value of the shares on the vesting date over (ii) the cash consideration (if any) paid for the shares. The participant may, however, elect under Section 83(b) of the Code to include as ordinary income in the year the unvested shares are issued an amount equal to the excess of (a) the fair market value of those shares on the issue date over (b) the cash consideration (if any) paid for such shares. If the Section 83(b) election is made, the participant will not recognize any additional income as and when the shares subsequently vest.

We will be entitled to an income tax deduction equal to the amount of ordinary income recognized by the participant at the time such ordinary income is recognized by the participant.

Other Awards

Generally, no taxable income is recognized upon receipt of stock units (including RSUs), performance awards or cash awards. The holder will recognize ordinary income in the year in which the shares subject to the award are actually issued or in the year in which the award is settled in cash. The amount of that income will be equal to the fair market value of the shares on the date of issuance or the amount of the cash paid in settlement of the award, and the holder will be required to satisfy the tax withholding requirements applicable to the income.

We will be entitled to an income tax deduction equal to the amount of ordinary income recognized by the holder at the time the shares are issued or the cash amount is paid.

Deductibility of Executive Compensation

Section 162(m) of the Code limits the deductibility for federal income tax purposes of certain compensation paid to any "covered employee" in excess of $1 million. For purposes of Section 162(m), the term "covered employee" includes any individual who serves as chief executive officer, chief financial officer or one of the other three most highly compensated executive officers for 2017 or any subsequent calendar year (and beginning in 2027, also including the next five highest-compensated employees for the applicable year). It is expected that compensation deductions for any covered employee with respect to awards under the Second A&R 2023 Plan will be subject to the $1 million annual deduction limitation.

Vote Required

Approval of the Second A&R 2023 Plan requires the affirmative vote of a majority of the votes cast on this proposal. Because abstentions and broker non-votes, if any, are not counted as votes cast for or against this resolution, they will have no effect on the outcome of the vote.

THE BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" PROPOSAL NO. 2.

PROPOSAL 3

Ratification of the Selection of Independent Registered Public Accounting Firm

Our Audit Committee has selected Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2025, and has further directed that we submit the selection of Ernst & Young LLP for ratification by our stockholders at the Annual Meeting.

We are not required to submit the selection of our independent registered public accounting firm for stockholder approval, but are submitting our selection of Ernst & Young LLP for stockholder ratification as a matter of good corporate governance. If the stockholders do not ratify this selection, the Audit Committee will reconsider its selection of Ernst & Young LLP. Even if the selection is ratified, our Audit Committee may direct the appointment of a different independent registered public accounting firm at any time during the year if the Audit Committee determines that the change would be in our best interests.

The Audit Committee reviews and pre-approves all audit and non-audit services performed by our independent registered public accounting firm. The Audit Committee may delegate its pre-approval authority to one or more of its members and has delegated such authority to the Chairman of the Audit Committee; any pre-approval decisions made by the Chairman are reported to the Audit Committee at the next scheduled committee meeting. The Audit Committee may pre-approve specified audit-related services (assurance and related services that are reasonably related to the performance of the audit or review of our financial statements and that are traditionally performed by the independent auditor) as well as specified tax services that the Audit Committee believes would not impair the independence of the independent auditor, and that are consistent with rules on auditor independence established by the SEC and the Public Company Accounting Oversight Board (PCAOB). The Audit Committee may also pre-approve those permissible non-audit services classified as "all other services" that it believes are routine and recurring services and would not impair the independence of the independent auditor and are consistent with SEC and PCAOB rules on auditor independence. All requests or applications for services to be provided by the independent auditor will be submitted to the Chief Financial Officer and must include a detailed description of the services to be rendered. The Chief Financial Officer or the Principal Accounting Officer, as the case may be, will authorize those services that have been pre-approved by the Audit Committee. If there is any question as to whether a proposed service fits within the pre-approved categories of services, the Chairman of the Audit Committee is to be consulted for a determination. For services that have not been pre-approved by the Audit Committee, requests or applications to provide services will be submitted to the Audit Committee by both the independent auditor and the Chief Financial Officer, and must include a joint oral or written statement as to whether, in their view, the request or application is consistent with the SEC's and PCAOB's rules on auditor independence.

All services rendered by Ernst & Young LLP in fiscal 2024 were approved in accordance with these policies. In its review of non-audit services, the Audit Committee considers, among other things, the possible impact of the performance of such services on the independent registered public accounting firm's independence. The Audit Committee has determined that the non-audit services performed by Ernst & Young LLP in the fiscal year ended December 31, 2024 were compatible with maintaining the independent registered public accounting firm's independence. Additional information concerning the Audit Committee and its activities can be found in the following sections of this Proxy Statement: "Board of Directors and Committees—Board Committees" and "Report of the Audit Committee."

Ernst & Young LLP has audited our financial statements since our inception. Representatives of Ernst & Young LLP are expected to be present at the Annual Meeting, will have the opportunity to make a statement if they desire to do so, and are expected to be available to respond to appropriate stockholder questions.

Fees for Independent Registered Public Accounting Firm

The following is a summary of the aggregate audit fees billed or expected to be billed by Ernst & Young LLP for the indicated fiscal years and the fees billed by Ernst & Young LLP for all other services rendered during the indicated fiscal years.

	2024	2023
Audit fees[1]	$ 2,820,000	$ 2,240,000
Audit-related fees	—	—
Tax fees[2]	93,000	77,000
All other fees	—	—
TOTAL	**$ 2,913,000**	**$ 2,317,000**

(1) Audit fees consist of the aggregate fees billed for professional services rendered for the audit of our annual financial statements included in our annual reports on Form 10-K; the review of our interim financial statements included in our quarterly reports on Form 10-Q; consultation on technical accounting matters; assistance with registration statements filed with the SEC; and the issuance of comfort letters and consents.

(2) Tax fees principally include fees for tax compliance and tax advice.

Vote Required

Ratification of the selection of the independent registered public accounting firm requires the affirmative vote of a majority of the votes cast. Because abstentions and broker non-votes, if any, are not counted as votes cast for or against this proposal, they will have no effect on the outcome of the vote.

THE BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" PROPOSAL NO. 3.

Report of the Audit Committee

The Audit Committee evaluates auditor performance, manages relations with our independent registered public accounting firm, and evaluates policies and procedures relating to internal control systems. The Audit Committee operates under a written Audit Committee Charter that has been adopted by the Board, a copy of which is available on our website at *www.ultragenyx.com.* All members of the Audit Committee currently meet the independence and qualification standards for Audit Committee membership set forth in the listing standards and rules of Nasdaq and the SEC.

No member of the Audit Committee is a professional accountant or auditor. The members' functions are not intended to duplicate or to certify the activities of management and the independent registered public accounting firm. The Audit Committee serves a board-level oversight role in which it provides advice, counsel, and direction to management and the auditors on the basis of the information it receives, discussions with management and the auditors, and the experience of the Audit Committee's members in business, financial, and accounting matters.

The Audit Committee oversees our financial reporting process on behalf of the Board. Our management has the primary responsibility for the financial statements and reporting process, including our system of internal controls over financial reporting. In fulfilling its oversight responsibilities, the Audit Committee reviewed and discussed with management the audited financial statements included in the Annual Report on Form 10-K for the fiscal year ended December 31, 2024. This review included a discussion of the quality and the acceptability of our financial reporting, including the nature and extent of disclosures in the financial statements and the accompanying notes.

The Audit Committee discussed with our independent registered public accounting firm, which is responsible for expressing an opinion on the conformity of the audited financial statements with generally accepted accounting principles in the U.S., their judgments as to the quality and the acceptability of our financial reporting and such other matters as are required to be discussed with the Committee pursuant to applicable rules of the PCAOB and the SEC. The Audit Committee has received the written disclosures and the letter from the independent registered public accounting firm required by the applicable rules of the PCAOB regarding the independent accountant's communications with the Audit Committee concerning independence. The Audit Committee discussed with the independent registered public accounting firm their independence.

In addition to the matters specified above, the Audit Committee discussed with our independent registered public accounting firm the overall scope, plans, and estimated costs of their audit. The Audit Committee met with the independent registered public accounting firm periodically, with and without management present, to discuss the results of the independent registered public accounting firm's examinations, the overall quality of our financial reporting, and the independent registered public accounting firm's reviews of the quarterly financial statements and drafts of the quarterly and annual reports.

Based on the reviews and discussions referred to above, the Audit Committee recommended to the Board that our audited financial statements should be included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024.

Submitted by the Audit Committee of the Board of Directors

Matthew K. Fust, Chairperson
Michael Narachi
Corsee D. Sanders, Ph.D.

PROPOSAL 4

Advisory (Non-Binding) Vote to Approve the Compensation of our Named Executive Officers

Background

Section 14A of the Exchange Act, as adopted pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act (Dodd-Frank Act) requires that stockholders have the opportunity to cast an advisory (non-binding) vote to approve the compensation of our named executive officers (say-on-pay vote).

The say-on-pay vote is a non-binding vote on the compensation of our "named executive officers," as described in the Compensation Discussion and Analysis section, the tabular disclosure regarding such compensation, and the accompanying narrative disclosure, set forth in this Proxy Statement. The say-on-pay vote is not a vote on our general compensation policies, compensation of our Board, our compensation policies as they relate to risk management, or our pay ratio.

Our philosophy in setting compensation policies for executive officers has two fundamental objectives: (1) to attract and retain a highly-skilled team of talented executives and (2) to align our executives' interests with those of our stockholders by rewarding short-term and long-term performance and tying compensation to increases in stockholder value. The Compensation Committee believes that executive compensation should be directly linked to performance, including continuous improvements in corporate performance and accomplishments of our strategic plan that are expected to increase stockholder value. The Compensation Discussion and Analysis section starting on page 37 provides a more detailed discussion of the executive compensation program and compensation philosophy.

The vote under this Proposal No. 4 is advisory and therefore not binding on us, the Board, or our Compensation Committee. However, our Board, including our Compensation Committee, values the opinions of our stockholders and, to the extent there is any significant vote against this proposal, we will consider our stockholders' concerns and evaluate what actions may be appropriate to address those concerns. The Dodd-Frank Act requires us to hold the say-on-pay vote at least once every three years, and we have determined to hold a say-on-pay vote every year. Unless the Board modifies its policy on the frequency of holding say-on-pay advisory votes, the next say-on-pay vote will occur in 2026.

Stockholders will be asked at the Annual Meeting to approve the following resolution pursuant to this Proposal No. 4:

RESOLVED, that the stockholders of Ultragenyx Pharmaceutical Inc. approve, on an advisory basis, the compensation of the Company's "named executive officers" (as defined in the Company's definitive proxy statement for the 2025 Annual Meeting of Stockholders (the "Proxy Statement")), as such compensation is described in the Compensation Discussion and Analysis section, the tabular disclosure regarding such compensation, and the accompanying narrative disclosure, set forth in the Company's Proxy Statement.

Vote Required

Approval of this resolution requires the affirmative vote of a majority of the votes cast on this proposal. Because abstentions and broker non-votes, if any, are not counted as votes cast for or against this resolution, they will have no effect on the outcome of the vote.

THE BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" PROPOSAL NO. 4.

Corporate Governance

Director Independence

Our Board currently consists of eight members. Our Board has determined that Dr. Dunsire, Mr. Fust, Mr. Narachi, Dr. Ray, Dr. Sanders, Dr. Suliman, and Mr. Welch qualify as "independent" directors in accordance with Nasdaq listing requirements and rules. Dr. Kakkis is not considered independent because he is an employee of the Company. Under Nasdaq rules, the Board's determination of a director's independence considers objective tests, such as whether the director is, or has been within the last three years, an employee of the Company and whether the director or any of his or her family members has engaged in certain types of business dealings with us. Under Nasdaq rules, our Board also evaluates whether any relationships exist that, in the opinion of our Board, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these independence determinations, our Board reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Director Overboarding Policy

Our Board believes that all members of the Board must have sufficient time to focus on his or her Board duties. Our Corporate Governance Guidelines limit the total number of public company boards that a director may serve as follows:

- *Director who is not a public company Chief Executive Officer: five total public company boards*
- *Director who serves as a Chief Executive Officer of a public company: three total public company boards*

The Nominating and Corporate Governance Committee regularly assesses compliance with this policy as part of the director nomination process. All of our directors are currently in compliance with our policy.

Global Code of Conduct

We have adopted a Global Code of Conduct that applies to all of our employees, officers, and directors, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Our Global Code of Conduct is available on our website, *www.ultragenyx.com,* under the "Corporate Governance" subsection of the "Investors" tab. We intend to promptly disclose on our website any future changes or amendments to, or waivers of, to the Global Code of Conduct that we are required to disclose under applicable rules. Our Board is responsible for applying and interpreting the Global Code of Conduct in situations where questions are presented to it.

Insider Trading, Anti-Hedging and Anti-Pledging Policy

We have adopted insider trading policies and procedures governing the purchase, sale and other transactions in Ultragenyx securities by our directors, officers and employees, and other covered persons, or the Company itself, that we believe are reasonably designed to promote compliance with insider trading laws, rules and regulations, and Nasdaq listing rules, as applicable.

As part of these policies and procedures, we prohibit our directors, officers, employees and other covered persons from engaging in (a) short-term trading; (b) short sales; (c) transactions involving publicly traded options or other derivatives, such as trading in puts or calls with respect to Company securities; (d) hedging transactions; and (e) pledging Ultragenyx securities as collateral for a loan.

Stockholder Communications

Generally, stockholders who have questions or concerns regarding the Company should contact our Investor Relations department at (844) 280-7681. However, any stockholders who wish to address questions regarding our business or affairs directly with the Board, or any individual director, should direct his or her questions in writing to the Chairman of the Board, c/o Ultragenyx Pharmaceutical Inc., 60 Leveroni Court, Novato, California 94949. At the request of the Chairman of the Board, the Corporate Secretary reviews all correspondence addressed to the Chairman, organizes the correspondence, and provides it to the Chairman or to individual directors, as appropriate. Our independent directors have requested that certain items that are inappropriate or unrelated to the Board's duties, such as spam, junk mail, mass mailings, solicitations, resumes, and job inquiries not be provided to directors.

Board of Directors and Committees

During fiscal 2024, our Board met four times. Each of our current directors attended 100% of the aggregate meetings of the Board and meetings of the committees of which the director was a member in fiscal 2024 held during the period when the director served on the Board or the committees, as applicable.

The Board has a standing Audit Committee, Compensation Committee, Nominating and Corporate Governance Committee, and Research and Development Committee. All members of the Audit, Compensation, and Nominating and Corporate Governance Committees are non-employee directors whom the Board has determined are independent under applicable independence standards (including the heightened independence standards that apply to Audit Committee and Compensation Committee members).

Five of the directors serving at the time of the 2024 Annual Meeting attended such annual meeting. Each director who is up for election at an annual meeting of stockholders or who has a term that continues after such annual meeting is encouraged to attend the annual meeting of stockholders.

Board Leadership Structure

We currently separate the positions of Chairman of the Board and Chief Executive Officer, which allows our Chief Executive Officer, Dr. Kakkis, to focus on our day-to-day business, while allowing the Chairman of the Board, Mr. Welch, to lead the Board in its fundamental role of providing advice to and independent oversight of management. Independent oversight of management is an important goal of the Board, which is why our Corporate Governance Guidelines provide that a lead independent director will be appointed by the Board if the Chairman is not independent. Additionally, our Board recognizes the time, effort, and energy that the Chief Executive Officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our Chairman. Our Board also believes that the separation of the Chairman and Chief Executive Officer positions fosters a greater role for the independent directors in the oversight of our Company and active participation of the independent directors in setting agendas and establishing priorities and procedures for the work of our Board. The benefits of the separated Chairman and Chief Executive Officer positions are augmented by the independence of seven of our eight current directors, including our Chairman, and our independent Board committees that provide appropriate oversight in the areas described below. At executive sessions of independent directors, these directors can speak candidly on any matter of interest. The independent directors of the Board regularly meet in executive sessions, and met four times in 2024, and the Chairman presides at these sessions. We believe this structure provides effective oversight of our management and the Company.

The Board believes that its programs for risk oversight, as described under "Role of the Board in Risk Oversight" below, would be effective under a variety of leadership frameworks. Accordingly, the Board's risk oversight function did not significantly impact its selection of the current leadership structure.

Role of the Board in Risk Oversight

The Board has overall responsibility for the oversight of our risk management process, which is designed to support the achievement of organizational objectives, including strategic objectives, to improve long-term organizational performance, and enhance stockholder value. Risk management includes not only understanding company-specific risks and the steps management implements to manage those risks, but also assessing what level of risk is acceptable and appropriate for us, taking into account the immediacy of any such risks, and evaluating risks and circumstances across various timeframes, including the short, medium and long term. Management is responsible for establishing our business strategy, identifying and assessing the related risks, and implementing appropriate risk management practices. The Board periodically reviews our business strategy and management's assessment of the related risk and discusses with management the appropriate level of risk for us. The Board also periodically evaluates and discusses potential emerging risks with members of senior management as well as third-party advisors and experts. In 2024, the Board and the committees, as appropriate, reviewed with management the various risks and mitigation strategies related to cost containment strategies, prioritization of the Company's pipeline programs, cybersecurity risks and the Company's initiatives related to our Impact Report. The Board also delegates to Board committees oversight of selected elements of risk as set forth below.

Board Committees

Our Board currently has a standing Audit Committee, Compensation Committee, Nominating and Governance Committee and Research and Development Committee. Each of these committees operates under a written charter which sets forth the functions and responsibilities of the committee, a copy of which is available on our website at www.ultragenyx.com under the "Corporate Governance" subsection of the "Investors" tab.

Audit Committee	Key Responsibilities
Members: Matthew K. Fust (Chairperson) Michael Narachi Corsee D. Sanders, Ph.D. *All members of the Audit Committee satisfy the current independence and financial literacy standards promulgated by Nasdaq and the SEC, and the Board has determined that Mr. Fust qualifies as an "audit committee financial expert," as the SEC has defined that term in Item 407 of Regulation S-K* **Meetings held during 2024:** Six	The Audit Committee has been delegated the task of overseeing significant financial risks facing us and steps management has undertaken to mitigate these risks. The Audit Committee reports back to the Board regarding these risks. In 2024, the Audit Committee reviewed with management, in particular, the risks and mitigation strategies related to cybersecurity and the security programs related to our information technology systems. The Audit Committee is also responsible for the following: • Appoints, approves the compensation of, reviews the performance of, and assesses the independence of our independent registered public accounting firm • Approves audit and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm • Reviews the audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements • Reviews and discusses with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures and critical accounting policies • Discusses with management, and as applicable, the independent auditor, disclosure controls and procedures over environmental and sustainability reporting data and disclosures • Reviews the adequacy of our internal control over financial reporting; establishes policies and procedures for the receipt and retention of accounting-related complaints and concerns • Recommends whether our audited financial statements shall be included in our annual reports on Form 10-K • Prepares the audit committee report to be included in our annual proxy statements • Reviews all related-person transactions • Reviews policies related to financial risk assessment and management • Establishes, maintains, and oversees our Global Code of Conduct • Assists the Nominating and Corporate Governance Committee by overseeing our compliance program with respect to legal and regulatory requirements impacting areas of financial risk • Annually reviews and reassesses the adequacy of the Audit Committee charter and performs other duties, as specified in the charter

Compensation Committee	Key Responsibilities
Members: Michael Narachi (Chairperson) Deborah Dunsire, M.D. Daniel G. Welch *All members of the Compensation Committee satisfy the current Nasdaq and SEC independence standards* **Meetings held during 2024: Five**	The Compensation Committee has been delegated the task of overseeing risks related to our compensation policies and programs. In 2024, the Compensation Committee reviewed with management in particular the risks and mitigation strategies related to human capital management, succession planning for senior management positions, and strategies related to the Company's management of outstanding equity awards. The Compensation Committee is also responsible for the following: • Annually reviews and approves corporate goals and objectives relevant to the compensation of our executive officers • Evaluates the performance of our executive officers in light of such goals and objectives, and determines the compensation of our executive officers • Appoints, compensates, and oversees the work of any compensation consultant, legal counsel, or other advisor retained by the Compensation Committee • Conducts the independence assessment outlined in Nasdaq rules with respect to any compensation consultant, legal counsel, or other advisor retained by the Compensation Committee • Oversees, and has the authority to administer, our compensation and benefit plans • Oversees administration of our clawback policy • Reviews and approves our policies and procedures for the grant of equity-based awards • Reviews and makes recommendations to the Board with respect to director compensation • Reviews and discusses with management the compensation discussion and analysis, if any, to be included in our annual proxy statements or annual reports on Form 10-K • Oversees the maintenance and presentation to the Board of management's plans for succession to senior management positions • Annually reviews and reassesses the adequacy of the Compensation Committee charter and performs other duties, as specified in the charter

Nominating and Corporate Governance Committee	Key Responsibilities
Members: Shehnaaz Suliman, M.D. (Chairperson) Matthew K. Fust Daniel G. Welch *All members of the Nominating and Corporate Governance Committee satisfy the current Nasdaq and SEC independence standards* **Meetings held during 2024: Three**	The Nominating and Corporate Governance Committee has been delegated the task of overseeing all risks facing us, other than those overseen by the Audit Committee and by the Compensation Committee, and reporting back to the Board regarding the same. In 2024, the Nominating and Corporate Governance Committee reviewed with management, in particular, CEO succession planning, the risks and mitigation strategies related to matters covered in our Impact Report, our director search process and the Company's governance structure to assess the continued appropriateness of the classified board and other structural elements for the Company. The Nominating and Corporate Governance Committee is also responsible for the following: • Develops and recommends to the Board criteria for Board and committee membership • Establishes procedures for identifying and evaluating Board candidates, including nominees recommended by stockholders; identifies individuals qualified to become members of the Board • Recommends to the Board the persons to be nominated for election as directors and to each of the Board's committees • Develops and recommends to the Board a set of corporate governance guidelines • Oversees the maintenance and presentation to the Board of plans for succession to the position of Chief Executive Officer • Assists the Compensation Committee in its oversight of succession planning for other senior management positions • Oversees our compliance program • Recommends to the Board and reviews on regular basis with Board our corporate responsibility and sustainability matters relevant to our business • Annually reviews and reassesses the adequacy of the Nominating and Corporate Governance Committee charter and performs other duties, as specified in the charter

Research and Development Committee	Key Responsibilities
Members: Amrit Ray, M.D. (Chairperson) Emil D. Kakkis, M.D., Ph.D. Deborah Dunsire, M.D. Corsee D. Sanders, Ph.D. Shehnaaz Suliman, M.D. **Meetings held during 2024:** Two	The Research and Development Committee assists the Board in its oversight of the strategic direction for our pipeline and investment in research and development. In 2024, the Research and Development Committee reviewed with management in particular the risks and mitigation strategies related to the Company's prioritization of its clinical and pre-clinical programs. The Research and Development Committee is also responsible for the following: • Evaluates and advises on our key R&D activities and early pipeline development goals and strategy • Evaluates and provides input with respect to the quality of the science being conducted and overall program execution • Assesses the overall quality of the R&D programs and prospects for progression to monitor our pipeline to maintain product flow • Evaluate and advise on our clinical-stage pipeline and the development strategies • Performs other duties as specified in the Research and Development Committee Charter

Compensation Committee Interlocks and Insider Participation

During fiscal 2024, the Compensation Committee consisted of Dr. Dunsire and Messrs. Narachi and Welch. None of the members of our Compensation Committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our Board or Compensation Committee.

Impact Report

At Ultragenyx, our purpose is to lead the future of rare disease medicine as we seek to treat individuals afflicted by diseases with limited or no treatment options, and we recognize that their lives and well-being are dependent upon our collective efforts to develop new therapies. For this reason, we are passionate about developing these therapies with the utmost urgency and care. Our strong commitment to ethics, integrity and responsible business practices is centered around partnering with the rare disease community, improving access to treatments, maintaining a people-first culture, and investing in innovation.

Our Impact Report for fiscal 2024 (2024 Impact Report) will be available in digital format on our website at www.ultragenyx.com under "Ultra-Committed – Corporate Responsibility". Website references throughout this document are provided for convenience only, and the content on the referenced websites is not incorporated by reference into this document. Our 2024 Impact Report is based on our strategic framework, which centers on six pillars: Innovation, Patients, People, Communities, Planet and Governance. The contents of our Impact Report are not deemed to be part of this Proxy Statement or incorporated by reference herein.

Executive Officers

Our current executive officers, their respective ages as of the date of this Proxy Statement, and positions are set forth in the following table. Biographical information regarding each executive officer (other than Dr. Kakkis) is set forth following the table. Biographical information for Dr. Kakkis is set forth above under Proposal No. 1 (Election of Class III Directors).

Name	Age	Position
Emil D. Kakkis, M.D., Ph.D.	64	President and Chief Executive Officer, Director
Eric Crombez, M.D.	52	Chief Medical Officer and Executive Vice President
Erik Harris	55	Chief Commercial Officer and Executive Vice President
Howard Horn	47	Chief Financial Officer, Corporate Strategy and Executive Vice President
Dennis Huang	60	Chief Technical Operations Officer and Gene Therapy Operations and Executive Vice President
Thomas Kassberg	64	Chief Business Officer and Executive Vice President
Karah Parschauer	47	Chief Legal Officer & Corporate Affairs and Executive Vice President
John R. Pinion II	58	Chief Quality Officer and Executive Vice President of Translational Sciences

Dr. Eric Crombez has served as our Chief Medical Officer, Executive Vice President since March 2023. Dr. Crombez previously served as our Chief Medical Officer for gene therapy and inborn errors of metabolism, overseeing global clinical development and execution for the Company's gene therapy programs, after he joined the Company following the acquisition of Dimension Therapeutics, a biotechnology company, in November 2017. At Dimension Therapeutics, Dr. Crombez served as Chief Medical Officer from December 2014 to November 2017 where he led the clinical development efforts for clinical gene therapy programs in hemophilia B, hemophilia A, ornithine transcarbamylase (OTC) deficiency and glycogen storage disease type Ia (GSDIa). Previously, he worked at Shire plc, a biopharmaceutical company, in its Human Genetics Therapy business unit. Dr. Crombez is an appointed industry representative on the FDA Cellular, Tissue and Gene Therapies Advisory Committee. He previously served as assistant professor, Department of Pediatrics, Division of Medical Genetics at the David Geffen School of Medicine at the University of California, Los Angeles (UCLA). Dr. Crombez currently serves on the board of directors of Abeona Therapeutics Inc., a publicly traded biopharmaceutical company. Dr. Crombez is a board-certified clinical geneticist and completed residencies in pediatrics and medical genetics and a fellowship in clinical biochemical genetics at the UCLA School of Medicine. Dr. Crombez obtained his B.S. in biology from the University of Michigan, Ann Arbor, and his M.D. from Wayne State University School of Medicine, Detroit.

Erik Harris has served as our Chief Commercial Officer and Executive Vice President since June 2019. Prior to his appointment as our Chief Commercial Officer, Erik served as our Senior Vice President and Head of North American Commercial Operations from July 2017 to June 2019. Prior to Ultragenyx, Mr. Harris spent six years at Crescendo Bioscience, Inc., a molecular diagnostic company, most recently as Vice President of Commercial. Earlier in his career, Mr. Harris served as Vice President of Marketing at InterMune, Inc., a biotechnology company, and also held positions in the commercial organizations at Elan Pharmaceuticals, Inc., Genentech, Inc., and Bristol-Myers Squibb Company. At the start of his professional career, Mr. Harris served as a Lieutenant Commander in Naval Aviation and Congressional Fellow for the United States Navy. Mr. Harris currently serves on the board of directors of Denali Therapeutics Inc. and Inozyme Pharma, Inc., each a publicly traded biopharmaceutical company. Mr. Harris holds a B.S. from the United States Naval Academy and an M.B.A. from the Wharton School of Business.

Howard Horn has served as our Chief Financial Officer, Corporate Strategy and Executive Vice President since October 2023. He previously served as Chief Financial Officer and as a member of the founding management team at Vir Biotechnology, a public biotech company from March 2017 to April 2023, where he led the accounting, finance, investor relations and facilities functions. Prior to Vir Biotechnology, Mr. Horn was at Biogen, a biotechnology company, where he served first as Vice President, Strategic Corporate Finance and led Biogen's corporate capital allocation processes, and then as Vice President, Business Planning and led Biogen's resource allocation processes across all functions and regions. Previously, he held positions of increasing responsibility as a consultant in the Pharmaceutical and Medical Products Practice at McKinsey & Company, and as an equity research analyst in the Life Sciences group at UBS Group AG. Mr. Horn received his B.A. in Economics from Princeton University and his M.B.A. from the Wharton School of the University of Pennsylvania.

Dennis Huang has served as our Executive Vice President since January 2016, our Chief Technical Operations Officer since May 2015 and as our Chief Technical Operations Officer and Gene Therapy Operations since December 2021. From May 2015 to January 2016, he served as our Senior Vice President. Prior to Ultragenyx, Mr. Huang served as Senior Vice President of Manufacturing and Supply Chain at InterMune, Inc., a biotechnology company, from August 2013 to March 2015. Prior to InterMune, Mr. Huang served as Vice President of Biologic Manufacturing and Development at Allergan, Inc., a global pharmaceutical company, from May 2006 to August 2013. Mr. Huang currently serves on the board of directors of CytoDel, Inc., a private biopharmaceutical company. Mr. Huang holds a B.A. in Chemistry from Knox College in Galesburg, Illinois.

Thomas Kassberg has served as our Executive Vice President since January 2016 and our Chief Business Officer since November 2011. From November 2011 to January 2016, he served as our Senior Vice President. Prior to Ultragenyx, Mr. Kassberg worked as Vice President of Business Development at Corium International, Inc., a biotechnology company, from July 2010 to October 2011. Prior to his work at Corium

International, Inc., Mr. Kassberg worked as an independent consultant in corporate development and business strategy and consulted with a number of companies from March 2009 to June 2010, including Corium International, Inc., a biopharmaceutical company, and Rib-X Pharmaceuticals, Inc., a pharmaceutical company focused on the development of novel antibiotics. Before becoming a consultant, Mr. Kassberg worked at Proteolix, Inc., a biotechnology company subsequently acquired by Onyx Pharmaceuticals, from January 2008 to February 2009, where he served as Senior Vice President of Corporate Development. Mr. Kassberg currently serves on the board of directors of Passage Bio, Inc., a publicly traded biotechnology company. Mr. Kassberg holds a B.A. in Business Administration from Gustavus Adolphus College and an M.B.A. from Northwestern University.

Karah Parschauer has served as our Chief Legal Officer & Corporate Affairs, Executive Vice President since February 2023, as our Chief Legal Officer and Executive Vice President since December 2021 and as our General Counsel and Executive Vice President since June 2016. Prior to Ultragenyx, Ms. Parschauer served in various executive capacities, and most recently as Vice President, Associate General Counsel, at Allergan plc, a pharmaceutical company, from June 2005 to June 2016. Prior to Allergan, Ms. Parschauer was an attorney at Latham & Watkins LLP, where she practiced in the areas of mergers and acquisitions, securities offerings and corporate governance. Ms. Parschauer currently serves on the board of directors of Evolus, Inc., a publicly traded performance beauty company, and the board of directors of Tenaya Therapeutics, a publicly traded biotechnology company. Ms. Parschauer holds a B.A. in Biology from Miami University and a J.D. from Harvard Law School.

John R. Pinion II has served as our Chief Quality Officer and Executive Vice President of Translational Sciences since September 2017. From January 2016 to September 2017, he served as our Executive Vice President of Analytical Sciences and Research, and from July 2015 to September 2017, as our Chief Quality Operations Officer. From July 2015 to January 2016, he served as our Senior Vice President of Analytical Sciences and Research. Prior to Ultragenyx, Mr. Pinion served in various roles with increasing responsibilities at Genentech, a pharmaceutical company, from 2005 to June 2015, including his most recent position as the Senior Vice President and Global Head of Quality and Compliance for Roche/Genentech Pharma Technical Operations from October 2009 to July 2015. Mr. Pinion currently serves on the board of directors of Aroa Biosurgery, a soft tissue regeneration company listed on the Australian Securities Exchange. Mr. Pinion holds a B.S. in Mechanical Engineering from the University of West Virginia.

Certain Relationships and Related-Person Transactions

Related-Person Transactions

Since January 1, 2024, we have not become, and are not currently proposed to be, a participant in any transactions required to be disclosed in the Proxy Statement under SEC rules with any "related persons," which are generally considered to be our directors and executive officers, nominees for director, holders of more than 5% of our outstanding common stock, and members of their immediate families.

Procedures for Related-Person Transactions

We have adopted a written related-person transactions policy that governs the review, approval, and/or ratification of transactions with a related person where the amount involved exceeds $100,000 and in which any related person has or will have a direct or indirect interest. Under the policy, a "related person" is defined as any person described in Item 404(a) of Regulation S-K and includes any director, nominee for director, or executive officer of the Company; a beneficial owner of more than five percent of any class of our voting securities; and a person who is an immediate family member of any such director, nominee for director, executive officer, or more-than-five percent beneficial owner (the term "immediate family member" includes any child, stepchild, parent, stepparent, spouse, sibling, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law and any person (other than a tenant or employee) sharing the household of any such director, nominee for director, executive officer, or more-than-five percent beneficial owner).

Pursuant to this policy, prior to entering into a transaction with a related person, our Chief Financial Officer (or Chief Legal Officer, in the case where the Chief Financial Officer has a direct or indirect interest in the transaction) will review the proposed transaction to determine if such transaction qualifies as a related-person transaction. If the Chief Financial Officer (or Chief Legal Officer, if applicable) determines that the proposed transaction is a related-person transaction, then the proposed transaction will be submitted to the Audit Committee for consideration at the next Audit Committee meeting; provided, however, that if the Chief Financial Officer (or Chief Legal Officer, if applicable), in consultation with the Chief Executive Officer, determines that it is not practicable or desirable to wait until the next meeting of the Audit Committee, then the Chief Financial Officer (or Chief Legal Officer, if applicable) shall submit the proposed transaction to the chairperson of the Audit Committee (who possesses delegated authority to act between meetings of the Audit Committee to pre-approve or ratify, as applicable, any related-person transaction in which the aggregate amount involved is expected to be less than $1 million).

In the event that our Chief Executive Officer or Chief Financial Officer (or Chief Legal Officer, if applicable) becomes aware of a related-person transaction that has not been previously approved or previously ratified under our related-person transaction policy, the transaction, if pending or ongoing, will be promptly submitted to the Audit Committee or the chairperson of the Audit Committee for consideration. If the transaction is already completed, the Audit Committee or the chairperson of the Audit Committee shall evaluate the transaction to determine if rescission of the transaction and/or any disciplinary action is appropriate.

In evaluating these transactions, the Audit Committee or the chairperson of the Audit Committee, as applicable, will consider all of the relevant facts and circumstances available, including (if applicable) but not limited to: the benefits to us; the impact on a director's independence in the event the related person is a director, an immediate family member of a director, or an entity in which a director has a position or relationship; the availability of other sources for comparable products or services; the terms of the transaction; and the terms available to unrelated third parties or to employees generally. The Audit Committee or the Chairperson of the Audit Committee, as applicable, will only approve related-person transactions that are in, or are not inconsistent with, the best interests of the Company and its stockholders, as the Audit Committee or the Chairperson of the Audit Committee determines in good faith.

No member of the Audit Committee shall participate in any review, consideration or approval of any related-person transaction with respect to which such member or any of his or her immediate family members is the related person.

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth information relating to the beneficial ownership of our common stock as of March 7, 2025 (unless otherwise indicated in the footnotes), by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock;
- each of our directors and nominees;
- each of our named executive officers; and
- all current directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the person has sole or shared voting power or investment power as well as any shares that the person has the right to acquire within 60 days through the exercise of any stock options, warrants or other rights. We believe, based on the information furnished to us, that except as otherwise indicated, and subject to applicable community property laws, the persons named in the table below have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 93,892,528 shares of our common stock outstanding as of March 7, 2025. Shares of our common stock that a person has the right to acquire within 60 days are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Ultragenyx Pharmaceutical Inc., 60 Leveroni Court, Novato, California 94949.

	Beneficial Ownership	
Name and Address of Beneficial Owner	**Number of Shares**	**% of Total**
Stockholders Owning Greater than 5%:		
The Vanguard Group[(1)]	8,673,432	9.2%
BlackRock, Inc.[(2)]	5,238,400	5.6%
Directors and Named Executive Officers:		
Deborah Dunsire, M.D.[(3)]	70,210	*
Matthew K. Fust[(4)]	61,590	*
Michael Narachi[(5)]	68,335	*
Amrit Ray, M.D.[(6)]	35,160	*
Corsee D. Sanders, Ph.D.[(7)]	27,274	*
Shehnaaz Suliman, M.D.[(8)]	61,585	*
Daniel G. Welch[(9)]	68,335	*
Emil D. Kakkis, M.D., Ph.D.[(10)]	3,293,909	3.5%
Eric Crombez, M.D.[(11)]	98,113	*
Erik Harris[(12)]	184,922	*
Howard Horn[(13)]	78,344	*
John R. Pinion II[(14)]	336,097	*
All current executive officers and directors as a group[(15)] (15 persons)	5,261,347	5.5%

* Indicates beneficial ownership of less than 1% of the total outstanding common stock.

(1) Based on information set forth in a Schedule 13G/A filed with the SEC on February 13, 2024 by The Vanguard Group. The Schedule 13G/A reported that, as of December 29, 2023, The Vanguard Group has shared voting power with respect to 33,125 shares, sole dispositive power with respect to 8,556,929 shares, and shared dispositive power with respect to 116,503 shares. The principal business address for The Vanguard Group is listed in such filing as 100 Vanguard Blvd., Malvern, PA 19355.

(2) Based on information set forth in a Schedule 13G/A filed with the SEC on January 29, 2024 by BlackRock, Inc. The Schedule 13G/A reported that, as of December 31, 2023, BlackRock, Inc. has sole voting power with respect to 4,967,673 shares and sole dispositive power with respect to 5,238,400 shares. The principal business address for BlackRock Inc. is listed in such filing as 50 Hudson Yards, New York, NY 10001.

(3) Consists of (a) 19,730 shares of common stock, (b) 50,480 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(4) Consists of (a) 14,860 shares of common stock and (b) 46,730 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(5) Consists of (a) 21,605 shares of common stock and (b) 46,730 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(6) Consists of (a) 10,573 shares of common stock and (b) 22,880 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table, and (c) 1,707 shares of common stock issuable pursuant to the vesting of RSUs within 60 days of the date of this table.
(7) Consists of (a) 6,664 shares of common stock and (b) 20,610 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(8) Consists of (a) 14,855 shares of common stock and (b) 46,730 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(9) Consists of (a) 21,605 shares of common stock and (b) 46,730 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(10) Consists of (a) 2,158,985 shares of common stock held by the Emil Kakkis and Jenny Soriano Living Trust, dated June 18, 2009, (b) 533,532 shares of common stock held by Dr. Kakkis and (c) 601,392 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table 4. Dr. Kakkis shares voting and dispositive power over the 2,158,985 shares of common stock held by the Emil Kakkis and Jenny Soriano Living Trust, dated June 18, 2009; each of Dr. Kakkis and Dr. Soriano is a trustee of such trust. Dr. Kakkis has sole voting and dispositive power over the 533,532 shares of common stock held by him and the 2,158,985 shares of common stock issuable pursuant to stock options held by Dr. Kakkis.
(11) Consists of (a) 32,081 shares of common stock and (b) 64,367 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table, and (c) 1,665 shares of common stock issuable pursuant to the vesting of RSUs within 60 days of the date of this table.
(12) Consists of (a) 41,992 shares of common stock and (b) 142,930 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(13) Consists of (a) 15,692 shares of common stock and (b) 62,652 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(14) Consists of (a) 66,084 shares of common stock and (b) 270,013 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this table.
(15) Consists of (a) 3,300,328 shares of common stock, (b) 1,957,647 shares of common stock issuable pursuant to stock options that are exercisable within 60 days of the date of this table, and (c) 3,372 shares of common stock issuable pursuant to the vesting of RSUs within 60 days of the date of this table.

Executive Compensation

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Compensation Discussion and Analysis

The following compensation discussion and analysis describes the material elements of compensation earned in fiscal 2024 by each of the executive officers identified below, who are referred to collectively as our "named executive officers." Our named executive officers with respect to the fiscal year that ended on December 31, 2024 are:

EMIL D. KAKKIS, M.D., PH.D.
President and Chief Executive Officer

HOWARD HORN
Chief Financial Officer, Corporate Strategy and Executive Vice President

ERIK HARRIS
Chief Commercial Officer and Executive Vice President

ERIC CROMBEZ, M.D.
Chief Medical Officer and Executive Vice President

JOHN R. PINION II
Chief Quality Officer and Executive Vice President of Translational Sciences

These persons constitute our principal executive officer, our principal financial offer and our three other most highly paid executive officers serving during fiscal 2024.

Business Highlights

2024 was a pivotal year for the Company as we expanded access and grew revenue from our four global commercial products while also advancing our six late-stage programs in serious genetic conditions. The following company performance highlights from the year directly contributed to achievement under our 2024 annual incentive program.

Financial and Commercial Highlights in 2024

- Raised our total revenue guidance in mid-2024 to the range of $530 million to $550 million and exceeded the upper end of the revised guidance range with total revenue of $560 million for the year. Total revenue in 2024 represented 29% growth compared to 2023.
- Generated 2024 Crysvita® product sales from Latin America and Turkey, where we lead commercialization activities of $135 million, representing 78% growth compared to 2023.
- Continued commercial expansion outside of the United States with Evkeeza® launches in Canada, Europe and Japan.

Clinical Program Highlights in 2024

- *UX143 for the treatment of Osteogenesis Imperfect (OI).*
  - Announced positive 14-month results from the Phase 2 portion of the ongoing Phase 2/3 *Orbit* study demonstrating that, as of the 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 and also resulted in ongoing and meaningful improvements in lumbar spine bone mineral density at month 12 without evidence of plateau.
  - Received Breakthrough Designation from the FDA as a treatment to reduce the risk of fracture associated with OI Type I, III, or IV in patients 2 years of age and older.
- *GTX-102 for the treatment of Angelman syndrome*
  - Announced positive interim data from the Phase 1/2 study reflecting that as of the data cut-off date, patients in the 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. As of the data cut-off date, treatment of the Dose Escalation Cohorts 4-7 showed long-term increasing and sustained clinical benefit far exceeding natural history data at Day 758.
  - Began enrollment in our global Phase 3 *Aspire* study.

- *UX111 for the treatment of Sanfilippo syndrome type A (MPS IIIA)*
  - Jointly sponsored a workshop with the Regan-Udall Foundation for the FDA on qualifying biomarkers to support accelerated approval in rare disease drug development – an example of the way we are leading and driving changes in the field of rare disease.
  - Submitted our BLA to the FDA, which was subsequently accepted and granted priority review by the FDA, positioning UX111 to becoming our first commercialized gene therapy product, if approved.
- *DTX401 for the treatment of Glycogen Storage Disease Type Ia, or GSDIa*
  - Announced positive topline results in May 2024 from our Phase 3 *GlucoGene* study for the treatment of patients aged eight years and older with the study achieving 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 announced positive updated, longer-term Phase 3 data from the study.
- *UX701 for the treatment of Wilson disease*
  - Announced positive data from the dose-finding stage of the *Cyprus2+* study of UX701 that demonstrated clinical activity as well as improvements in copper metabolism for patients treated in Stage 1 of the study and our plans to initiate a fourth dose-finding cohort to enhance the efficiency and efficacy of the gene therapy.
- *DTX301 for the treatment of Ornithine Transcarbamylase, or OTC, deficiency*
  - Continued enrollment of our Phase 3 study of DTX301.

Stockholder Outreach

Stockholder Advisory Vote on Executive Compensation

Each year, our stockholders are provided the opportunity to cast an advisory vote on the compensation of our named executive officers, or the "say-on-pay" vote, and the Compensation Committee considers the outcome of the prior year's say-on-pay vote when making decisions relating to the compensation of our named executive officers and our executive compensation programs. We received 74% support for our say-on-pay proposal at our 2024 Annual Meeting. While this result reflects broad support of our compensation philosophy and pay practices, we were nevertheless disappointed by the outcome. In light of this result, we are continuing to engage with our stockholders as we have in prior years, reflecting our commitment to engagement, communication and transparency.

Stockholder Engagement

We regularly engage with our stockholders to solicit their feedback on a variety of topics, including our equity plan, executive compensation, corporate governance, corporate responsibility and other topics in order to gain a better understanding of their perspective on these issues. Stockholder feedback is important, and the information we glean from these engagements is highly valued. Stockholders also regularly meet with members of our senior management team to discuss our strategy and review our business, goals and performance. During our recent engagement season, we reached out to stockholders representing approximately 70% of our outstanding shares as of September 30, 2024, including almost all of our top 25 largest stockholders and met with those who responded to our engagement request, representing approximately 25% of our outstanding shares as of September 30, 2024. Participants at these meetings included our Chief Legal Officer, our Chief Human Resources Officer and Michael Narachi, an independent director and Chairperson of our Compensation Committee. Topics discussed during the meetings included our equity plan, executive compensation, corporate governance and sustainability matters. Our Board and management team reviewed and considered feedback received throughout our engagement activities and adopted certain changes in response to such feedback as described below.

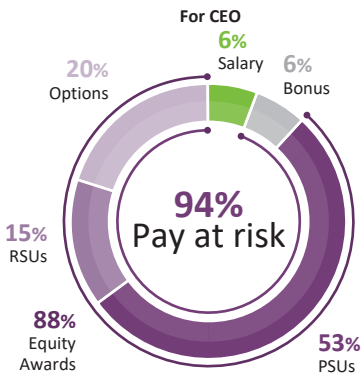
Outcomes from Engagement

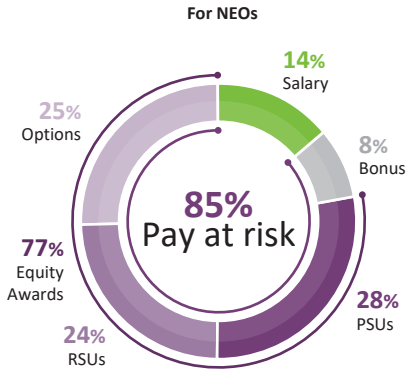
Feedback Received	Action Taken
More of executive's compensation should be based on performance and "at risk"	We have increased the percentage of PSUs from 33% to 50% for our executive officers (excluding our Chief Executive Officer) for the 2025 equity awards. For our Chief Executive Officer, we maintained the percentage of PSUs of 60% for 2024 and 2025 annual grants. We have also incorporated a "cap" on the portion of the PSUs subject to relative TSR performance for 2025 such that no more than the target number of PSUs may be earned if our absolute TSR is negative, regardless of our relative TSR performance.
Greater transparency related to corporate goals and goals achievement	We have included a more detailed summary regarding our bonus program and the impact of corporate goals and individual goals achievements on the bonus payout. We have also included additional detailed disclosure related to achievement of our corporate goals, including the achievement of each goal category. See the section below entitled "Annual Bonuses".

Compensation Highlights

As described below under "Compensation Philosophy and Objectives", our Compensation Committee believes that executive compensation should be directly linked to short-term and long-term performance and should result in long-term value creation for stockholders. A few of the key decisions made by the Compensation Committee aligned with such philosophy are as follows:

- ***Modest (or no) base salary adjustments in 2024; no base salary increase for CEO in 2025:*** Base salary increases in 2024 were 4% for Dr. Kakkis, our Chief Executive Officer, and 3% for each of Mr. Harris and Mr. Pinion. Mr. Horn who joined our company in October 2023 did not receive a base salary increase in 2024. Dr. Crombez received a base salary increase of 15% to align closer to the median for similar roles at peer companies. Salary increases were generally based on competitive market positioning and individual performance and were aligned to increases provided to all employees in good performance standing. In 2025, Dr.Kakkis opted not to receive a base salary increase.
- ***Increasing emphasis on performance-based awards:*** We maintained our equity mix at one-third of each PSUs, RSUs and stock options for named executive officers other than our Chief Executive Officer for 2024 annual grants but we increased the percentage of PSUs to 50% for the 2025 annual grant for our named executive officers (other than our Chief Executive Officer) without increasing the size of the pay package. For our Chief Executive Officer, PSUs were 60% of his annual grants in 2024 and 2025, consistent with the allocation implemented in 2023.
- ***Lengthening the time horizon for strategic performance portion of the PSUs:*** We lengthened the performance period for the strategic performance portion of the PSUs from two years to three years and, in doing so, we will require sustained performance over a longer-term timeframe.
- ***Increasing emphasis on relative TSR portion and the strategic performance portion of PSU awards:*** We shifted the PSU award mix to 1/3 for each of the revenue portion (decrease), strategic performance portion (increase), and relative TSR portion (increase) to add rigor and complexity to our PSU program.
- ***Further limit PSU upside:*** Beginning in 2025, the relative TSR portion of the PSUs is subject to a "cap" such that no more than the target number of PSUs may be earned if our absolute TSR is negative, regardless of our relative TSR performance.
- ***PSU payouts linked to performance:*** Our revenue portion of the 2023 PSUs paid out below target, at 74%.
- ***Pay mix is highly "at risk":*** The percentage of pay that is "at risk" for our CEO and named executive officers is 94% and 85%, respectively, helping us align pay with performance.

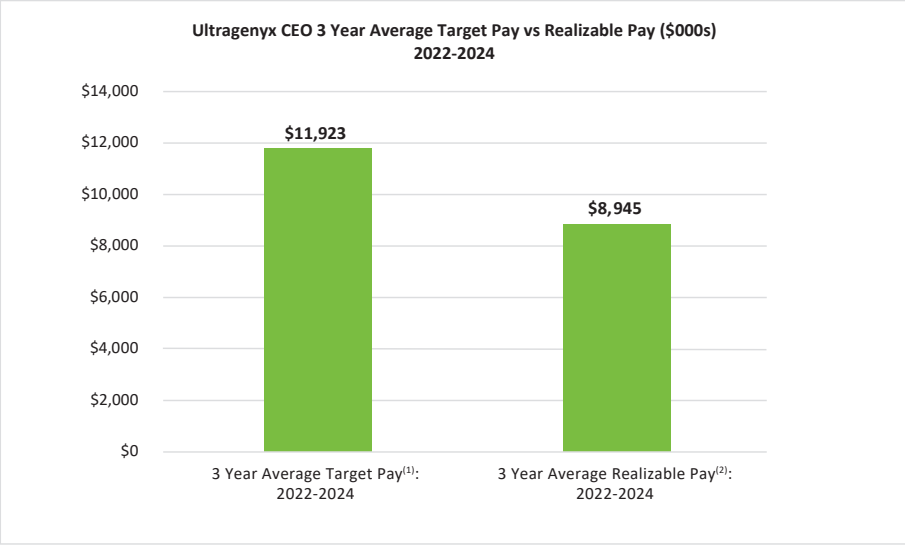




CEO Realizable Compensation

To ensure ongoing alignment to the compensation philosophy, in 2024 our Compensation Committee evaluated the relationship between the target and realizable value of the compensation granted to our CEO from 2022 through 2024.

The average realizable pay of our CEO over 2022 through 2024 is lower than the average target compensation for such three-year period, primarily as a result of the decrease in value of in-flight equity awards resulting from our stock performance as of the end of 2024 and the payouts from PSUs issued in 2022 and 2023 that paid out below target, as reflected in the following chart and described below.



(1) Target value represents the base salary rate in effect in each year, target annual bonus, and the grant date fair value of long-term incentive awards (PSUs and RSUs).

(2) Realizable value is calculated as the sum of the compensation deliverable in each year, including actual salary paid, annual bonus earned, and the value of long-term incentive plan components (PSUs, RSUs, and stock options) as valued on December 31, 2024 using our year-end stock price of $42.07 per share. The realizable value for PSUs granted in 2022 was adjusted to reflect the recent payout at 25% of target. The realizable value for PSUs granted in 2023 was adjusted to reflect recent payouts based on Revenue and Strategic performance, and the Relative TSR payout was assumed to be at 100% of target. The realizable value for PSUs granted in 2024 (for which the performance period has not ended) assumes payout at 100%.

Compensation Philosophy and Objectives

Our philosophy in setting compensation policies for executive officers has two fundamental objectives: (1) to attract and retain a highly-skilled team of executives and (2) to align our executives' interests with those of our stockholders by rewarding short-term and long-term performance and tying compensation to increases in stockholder value. The Compensation Committee believes that executive compensation should be directly linked to both continuous improvements in corporate performance (pay for performance) and accomplishments that are expected to increase stockholder value. In furtherance of this goal, the Compensation Committee has adhered to the following guidelines as a foundation for decisions that affect the levels of compensation:

- provide a competitive total compensation package that enables us to attract and retain highly qualified executives with the skills and experience required for the achievement of business goals;
- align compensation elements with our annual goals and long-term business strategies and objectives;
- promote the achievement of key strategic and financial performance measures by linking short-term and long-term cash and equity incentives to the achievement of measurable corporate and individual performance goals and objectives; and
- align executives' incentives with the creation of stockholder value.

The Compensation Committee has historically compensated executive officers with three primary compensation components: a base salary, an annual bonus opportunity, and equity-based compensation. The Compensation Committee believes that cash compensation in the form of base salary and an annual bonus opportunity provides our executive officers with short-term rewards for success in achieving annual goals and objectives, and that long-term compensation through the award of stock options, RSUs and PSUs aligns the objectives of management with those of our stockholders with respect to long-term performance and success of the Company.

In setting compensation levels for our executive officers, the Compensation Committee does not formulaically benchmark against any one specific reference point. Instead, it considers a variety of factors, including peer group survey data, tenure, role, responsibilities, performance, and competitive market practices. Compensation paid to our named executive officers is delivered primarily through at-risk pay, based on both short-term and long-term incentives, including the achievement of corporate and individual goals and objectives.

In addition to our compensation elements, the following compensation program features are designed to align our executive team's interests with stockholder interests and market best practices.

What We Do	What We Don't Do
Our Compensation Committee is comprised solely of independent directors.	We do not offer any tax gross-up payments to our executive team for any change-of-control payments.
Our Compensation Committee engages its own independent, external compensation consultant to assist the committee in its review of executive and director compensation practices.	As discussed above under "—Corporate Governance", we prohibit our employees, including our executive officers, from hedging our securities.
We proactively engage with our stockholders throughout the year.	We prohibit our employees, including our executive team, from pledging our securities.
We have a clawback policy that permits recovery of all incentive compensation (including time-based and performance-based equity awards) in the event of fraud or intentional misconduct by our current or former executive officers; see "—Clawback Policy".	We do not offer our executive team any substantially enhanced benefits or perquisites when compared with our overall employee population.
We require our executive officers and directors to hold shares of our common stock in order to align their long-term interests with those of our stockholders; see "—Minimum Stock Ownership Requirements".	We prohibit the repricing of outstanding stock options without stockholder approval.
We have double-trigger vesting of outstanding equity awards following covered transactions under our employment arrangements with our executive officers. See "Summary Compensation Table—Narrative Disclosure to Summary Compensation Table—Covered Transaction".	The Second A&R 2023 Plan does not include an "evergreen" feature.
We have established a long-term incentive program applicable to all current employees, including our executive officers, to further tie compensation to performance and focus employee efforts on corporate goals and objectives; see "—Equity Compensation—Annual Equity Grants in Fiscal 2024" and "—Fiscal 2025 Compensation – Equity Grants."	
We hold an annual say-on-pay vote for stockholders.	

Roles in Determining Compensation

Compensation Committee

The Board has delegated to the Compensation Committee the responsibility to ensure that total compensation paid to our executive officers, including our named executive officers, is consistent with our compensation policy and objectives. The Compensation Committee oversees and approves all compensation arrangements and actions for our executive officers, including our named executive officers. While the Compensation Committee draws on a number of resources, including input from the Board, the Chief Executive Officer, and its independent compensation consultants, to make decisions regarding our executive compensation program, ultimate decision-making authority rests with the Compensation Committee. The Compensation Committee retains discretion over base salaries, annual bonuses, and equity compensation for executive officers. The Compensation Committee relies upon the judgment of its members in making compensation decisions, after reviewing our corporate performance and carefully evaluating an executive's performance during the year against established goals, operational performance, and business responsibilities. In addition, the Compensation Committee utilizes discretion in the assessment process to respond to and adjust to a dynamic business environment. The Compensation Committee may delegate its authority to one or more subcommittees. The Compensation Committee may also delegate authority to review and approve the compensation of our employees to certain of our executive officers, including the grant of equity awards under the 2023 Plan (as amended and restated).

Compensation Consultant

The Compensation Committee retains the services of an independent, external compensation consultant, Aon's Human Capital Solutions Practice, a division of Aon plc (Aon). The mandate of the consultant is to assist the Compensation Committee in its review of executive and director compensation practices, including the competitiveness of pay levels, executive compensation design, benchmarking with our peers in the industry, and other technical considerations, including tax- and accounting-related matters. The Compensation Committee annually evaluates Aon's performance and determines whether to engage Aon or another compensation consultant and has the final authority to engage and terminate Aon's services. In 2024, the cost of Aon's consulting services related to executive compensation, director compensation and equity plan design and considerations provided to the Compensation Committee was approximately $208,597. In

addition, in 2024, management also engaged Aon to provide survey data relating to broad-based compensation matters. The aggregate cost of the survey data provided by Aon in 2024 was approximately $33,205. No other consulting services were provided by Aon or its affiliates to the Company in 2024.

Our Compensation Committee has assessed the independence of Aon consistent with Nasdaq listing standards and has concluded that the engagement of Aon does not raise any conflict of interest.

Chief Executive Officer

The Chief Executive Officer, and other executive officers, attends Compensation Committee meetings and works with the Compensation Committee Chairman and Aon to develop compensation recommendations for the executive officers (excluding the Chief Executive Officer), based upon individual experience and breadth of knowledge, internal considerations, individual performance during the fiscal year, competitive market considerations, and other factors deemed relevant by the Compensation Committee. The recommendations are then submitted to the Compensation Committee for review and consideration. The Compensation Committee works directly with Aon and the other non-employee directors of the Board to evaluate the performance of the Chief Executive Officer and determine compensation actions for the Chief Executive Officer, and the Chief Executive Officer does not participate in the portions of meetings in which his compensation is discussed and determined.

Defining and Comparing Compensation to Peer Group Benchmarks

While we do not establish compensation levels based solely on benchmarking, pay practices at other companies are an important factor that the Compensation Committee considers in assessing the reasonableness of compensation and ensuring that our compensation practices are competitive in the marketplace. Market data is one element considered by the Compensation Committee when making executive compensation decisions, but the Compensation Committee does not set compensation levels based solely on market data. Rather, the Compensation Committee reviews the 25th, 50th and 75th percentiles of relevant market data as one frame of reference in making its executive compensation decisions. Final executive compensation decisions reflect a variety of factors, including each executive's experience, performance rating, the relative importance of the executive's role within the organization, as well as where each executive's pay level falls relative to the market data.

In order to evaluate the level of compensation for our named executive officers for 2024, our Compensation Committee, using information provided by Aon, established a peer group of publicly traded, national, and regional companies in the biopharmaceutical and biotechnology industries based on a balance of the following criteria:

- companies with emphasis on orphan pharmaceutical products;
- companies with comparable market capitalizations (i.e., in the range of $2 billion to $16 billion);
- companies with revenue of between $200 million and $1.4 billion; and
- companies with headcounts between 300 to 4,000 employees.

Our 2024 peer group is comprised of the following 20 companies in the pharmaceutical and biotechnology industries, reflecting the removal of Alnylam Pharmaceuticals Inc., Biohaven Pharmaceutical Holding Company, Ltd., Global Blood Therapeutics, Inc. and United Therapeutics Corporation from our peer group used to evaluate compensation for our named executive officers in 2023 in order to add BridgeBio Pharma, Inc. Intra-Cellular Therapies Inc. and Sage Therapeutics, Inc. who our Compensation Committee determined better fit the balanced criteria described above.

ACADIA Pharmaceuticals Inc.	BridgeBio Pharma, Inc.	Ionis Pharmaceuticals, Inc.
Alkermes plc	Corcept Therapeutics Inc.	Jazz Pharmaceuticals plc
Amicus Therapeutics	Exelixis Inc.	Neurocrine Biosciences, Inc.
Apellis Pharmaceuticals, Inc.	FibroGen, Inc.	PTC Therapeutics, Inc.
BioCryst Pharmaceuticals, Inc.	Halozyme Therapeutics	Sage Therapeutics, Inc.
BioMarin Pharmaceutical Inc.	Insmed Incorporated	Sarepta Therapeutics, Inc.
Blueprint Medicines Corporation	Intra-Cellular Therapies Inc.	

We believe that the compensation practices of our 2024 peer group provided us with appropriate benchmarks for evaluating the compensation of our named executive officers for 2024 because of the developmental, market and organizational characteristics we shared with our peer group. At the time that we selected our 2024 peer group we were at approximately the 26th percentile of the peer group in terms of market capitalization, the 81st percentile in terms of employee headcount and the 44th percentile in terms of revenue.

Annual Performance Reviews

Our Compensation Committee conducts an annual performance review of our named executive officers and approves their compensation. By the end of the first quarter of each year, base salaries and equity awards for the fiscal year are approved and, for purposes of determining potential payments under our corporate bonus plan (the bonus plan), target bonuses, annual corporate goals and individual performance objectives are established and set forth in writing. After the end of each year, our Compensation Committee determines the amounts that will be paid to our executive officers under our bonus plan after carefully (1) reviewing overall corporate performance; (2) evaluating each named executive officer's annual performance against established corporate goals; and (3) in the case of executive officers other than our Chief Executive Officer, reviewing the achievement of individual performance objectives.

At its first regularly scheduled meeting each year, our Compensation Committee, with input from the Board, evaluates our Chief Executive Officer's individual performance, determines whether to adjust his base salary, and determines the amount of equity awards and his bonus, if any, under our bonus plan.

Our Compensation Committee may also review and adjust the compensation of our executive officers throughout the course of the year.

Base Salary

Overview

The Compensation Committee believes it is important to provide adequate fixed compensation to our executive officers working in a highly volatile and competitive industry. The Compensation Committee's choice of actual pay levels versus our competitive market reflects consideration of our stockholders' interests in paying what is necessary to achieve our corporate goals, while setting competitive levels which are essential to retain these key executives. In determining appropriate base salary levels for a given executive officer, the Compensation Committee considers the following factors:

- individual performance of, and overall management of the function by, the executive, as well as our overall corporate performance, during the prior year;
- level of responsibility, including breadth, scope, and complexity of the position;
- level of experience and expertise of the executive;
- internal review of the executive's compensation relative to other executives to ensure internal equity;
- executive officer compensation levels at other similar companies to ensure competitiveness; and
- recruiting and retention market dynamics.

The effective date of annual merit increases to base salary is March 1.

2024 Base Salaries

The Compensation Committee engaged Aon to conduct a competitive review and analysis of our current executive compensation program relative to our 2024 peer group. Aon prepared an Executive Compensation Assessment report in February 2024 that provided a competitive assessment of our executive compensation program as compared to the 2024 peer group data for base salaries, target total cash compensation, and equity compensation.

For 2024, base salary increases for our Chief Executive Officer was 4% annualized and approximately 3% annualized for Mr. Harris and Mr. Pinion. Mr. Horn who joined our company in October 2023 did not receive a base salary increase for 2024. Dr. Crombez received a base salary increase of 15% following an independent compensation market analysis, which identified that his prior base salary was below the median for similar roles at peer companies. This adjustment brought his salary into line with market norms for the position while ensuring competitiveness in attracting and retaining talent. The overall 2024 merit budget was based on an Aon trend report regarding projected market merit spends for 2024. Individual increases in base salaries were also based on achievement of 2023 individual goals.

The following table shows the increases in base salaries for our named executive officers between fiscal 2023 and fiscal 2024. Mr. Horn joined the Company in October 2023 and as such, did not receive an increase in his base salary for fiscal 2024.

Name	Title	Fiscal 2023 Base Salary (as of December 31, 2023)	Fiscal 2024 Base Salary (as of December 31, 2024)	Percentage Increase (%)
Emil D. Kakkis, M.D., Ph.D.	President and Chief Executive Officer	$ 828,000	$ 861,000	4.0
Howard Horn	Chief Financial Officer, Corporate Strategy and Executive Vice President	590,000	590,000	—
Erik Harris	Chief Commercial Officer and Executive Vice President	589,000	607,000	3.1
Eric Crombez, M.D.	Chief Medical Officer and Executive Vice President	525,000	604,000	15.0
John R. Pinion II	Chief Quality Officer and Executive Vice President, Translational Sciences	555,000	572,000	3.1

Annual Bonus

Overview

Our annual incentive program provides the opportunity for cash bonus awards based on the achievement of annual performance goals. For executive officers, other than the Chief Executive Officer, bonus awards are based on both corporate and individual performance, with corporate performance serving as the primary driver.

- Corporate performance goals focus on business, financial, and operational measures or objectives.
- Individual performance goals reflect an executive's contributions toward achieving corporate goals and leadership within their respective function.
- The Chief Executive Officer's bonus is entirely based on corporate performance.

At the beginning of each performance year, the Chief Executive Officer sets and communicates individual goals to each executive officer. At the end of the year, the Compensation Committee evaluates corporate performance and each executive officer's contributions (excluding the Chief Executive Officer) to determine whether a bonus will be awarded and, if so, the amount. The annual bonus is not guaranteed and is entirely at risk.

The Chief Executive Officer's annual bonus award is based 100% on corporate performance achievement.

For executive officers other than the Chief Executive Officer, the annual bonus is calculated as follows:

While individual performance is a key factor, corporate performance is the primary driver in the formula. If corporate goals are not met, an executive may not receive an annual bonus award, even if the executive performed well individually. Similarly, if corporate goals are met, an executive with low individual performance may receive a reduced award or no bonus award.

The corporate performance achievement percentage is capped at 150% and the individual performance achievement percentage is capped at 133%, resulting in a maximum bonus of 150% of target for the Chief Executive Officer and 200% of target for the other executive officers. The corporate performance score determines the overall bonus pool funding. If corporate performance achievement is at or below 50%, the corporate component of the bonus is not funded and no bonuses will be awarded, regardless of individual performance.

Actual payouts are at risk and contingent on both corporate and individual performance. Corporate performance payouts are based on the achievement of predefined goals, while individual performance is assessed across three key areas: attainment of individual goals, execution of key role deliverables, and demonstration of the Company's values and behaviors.

Subject to the rights contained in any agreement between the Company and the executive officer, an executive officer must be employed by the Company on the bonus payment date to be eligible to receive a bonus payment.

Fiscal 2024 Bonuses

Annual corporate goals for fiscal 2024 were proposed by our executive officers and approved by our Compensation Committee in early 2024. Individual objectives for our executive officers, other than the Chief Executive Officer, for 2024 were proposed by each executive officer, with review, input and confirmation from our Chief Executive Officer.

Each executive officer's annual target bonus is based on their role, responsibilities, accountability, potential impact on corporate performance and peer group benchmarks. The target bonuses, as a percentage of base salary, for the named executive officers for fiscal 2024 are set forth in the following table.

Name	Target Bonus for Fiscal 2024 (% of Base Salary)
Emil D. Kakkis, M.D., Ph.D.	80
Howard Horn	50
Erik Harris	50
Eric Crombez, M.D.	50
John R. Pinion II	50

In February 2025, the Compensation Committee assessed our overall 2024 performance against the achievement of the corporate goals to determine a total percentage of achievement between 0% and 150%. The Compensation Committee considered the following performance goals, as well as the relative weighting of these goals, in assessing overall performance for the 2024 fiscal year:

Goal (Weighting)	Key Results	Achievement Against Goal	Weighted Achievement
Commercial (30%) Revenue goals for commercial assets	***Exceeded.*** Achieved revenue targets between base and outperform	123%	**37%**
Development (60%) Clinical program-based goals focused on clinical development and enrollment-targets and milestone, including enrollment of the phase 3 portion of our study for UX143 and the BLA filing for UX111 by specified timelines. Highest weight was placed on goals related to GTX-102, UX143, UX701 and DTX401.	**Met.** Overall achievement of base target for development goals	100%	**60%**
People and Governance (10%)	**Met most.** As summarized below, met or exceeded goals related to culture and governance.	70%	**7.0%**
• *Budget:* Maintaining operating cash usage within 5% of budget (5%)	• **Did not meet.** Minimum target goal was not achieved primarily due to expenses from acceleration of select manufacturing and development activities as well as timing of certain cash flows (0% achievement)		
• *Culture:* Maintain high retention of employees in good performance standing (1.5%)	• **Exceeded.** Retention rate exceeded outperform target (150% achievement)		
• *Culture:* Goals related to maintaining and improving employee engagement, inclusion and well being (each 0.5%, together 1.5%)	• *Employee engagement:* **Met** base target for goal (100% achievement) • *Inclusion:* **Exceeded** outperform goal (150% achievement) • *Well-being:* **Met** base target for goal (100% achievement)		
• *Governance:* Goals related to continuous compliant and ethical practices (2%)	• **Exceeded.** Achieved outperform target goals (150% achievement)		

In establishing these goals, the Compensation Committee selected performance goals that it considered aggressive, meaning that they are goals that were considered achievable, but only with a high degree of diligence and success in execution.

In assessing performance against these goals, the Compensation Committee reviewed each goal and determined whether or not it was achieved. The Compensation Committee then referred to the relative importance of the goals, based on the previously established weightings of each goal. The Compensation Committee also considered additional key corporate achievements that were not represented in the 2024 corporate goals, including completion of a successful financing transaction and significant work to gain alignment with the FDA to support the submission of the BLA for UX111 for accelerated approval. For all goals combined, including additional achievements by the Company not previously defined, the Compensation Committee determined an overall 110% achievement for fiscal year 2024.

In February 2025, in addition to assessing the foregoing corporate goals, the Compensation Committee (after consultation with our Chief Executive Officer) assessed the individual accomplishments of our named executive officers for purposes of determining the individual component of their annual bonus, other than our Chief Executive Officer whose annual bonus is based solely on the corporate goals described above. Key individual achievements for these named executive officers are summarized below.

Named Executive Officer	Key 2024 Achievements
Howard Horn *Chief Financial Officer and EVP, Corporate Strategy*	• Successful execution of follow on equity offering for gross proceeds of $403 million • Informed decision making and drove execution of business development transactions, 2024 strategy and budget and long-range plan • Execution of defined operational excellence projects in collaboration with business teams
Erik Harris *Chief Commercial Officer and EVP*	• Achieved continued growth in product sales to support achievement of global revenue targets, including exceeding top range of revenue guidance • Executed commercial planning for launch readiness for late-stage programs • Retention of key contributors for commercial leadership team
Eric Crombez, M.D. *Chief Medical Officer and EVP*	• Led development team in achievement of high priority clinical milestones • Effective resource planning and right-sizing of development teams to achieve milestones • Continued close collaboration with cross-functional executive team to elevate development team performance and drive the business
John R. Pinion II *Chief Quality Officer and Executive Vice President, Translational Sciences*	• Led and sponsored non-clinical activities to enable development and advancement of translational science portfolio • Successfully led start-up and advancement of Amlogenyx operations and other specified pre-clinical development, per plan • Led reliable quality supply across commercial and clinical products to support patient needs, revenue growth and clinical program success

Dr. Kakkis evaluated the performance of Mr. Horn, Mr. Harris, Dr. Crombez and Mr. Pinion after considering the above achievements and provided a proposed bonus amount for each such officer to the Compensation Committee in light of such officer's achievements during 2024.

Achievement of Goals and Relationship to Compensation Awarded

The overall 110% achievement score for the 2024 corporate goals, combined with Dr. Kakkis' assessment of the individual performance and achievement of Mr. Horn, Mr. Harris, Dr. Crombez and Mr. Pinion during fiscal 2024 resulted in the Compensation Committee approving bonus awards for performance in 2024 as set forth in the following table. The bonuses awarded under our 2024 annual incentive program were paid in March 2025.

Name	Title	Corporate Component Score (%) (100% for CEO)	Individual Component Score (%)	Total Fiscal 2024 Bonus	Bonus Achieved (as % of Base Salary)
Emil D. Kakkis, M.D., Ph.D.	President and Chief Executive Officer	110	—	$ 757,768	88%
Howard Horn	Chief Financial Officer and Executive Vice President, Corporate Strategy	110	106	$ 343,970	58%
Erik Harris	Chief Commercial Officer and Executive Vice President	110	110	$ 367,235	61%
Eric Crombez, M.D.	Chief Medical Officer and Executive Vice President	110	115	$ 382,030	63%
John R. Pinion II	Chief Quality Officer and Executive Vice President, Translational Sciences	110	108	$ 339,768	59%

Equity Compensation

Overview

Stock Options, Restricted Stock Units and Performance Stock Units. Executive officers are eligible to receive equity compensation in the form of stock options, RSUs and/or PSUs. The Compensation Committee grants stock options, RSUs and/or PSUs annually to executive officers to recognize their contributions to the achievement of corporate objectives, to align their interests with those of our stockholders by creating value tied to the performance of our stock price, and for retention purposes. In determining the form and value of an annual grant, the Compensation Committee considers the contributions and responsibilities of each executive officer, appropriate incentives for the achievement of our long-term growth, the size and value of grants made to other executives at peer companies holding comparable positions, individual achievement of designated performance goals, and our overall performance relative to corporate objectives. The Compensation Committee also grants stock options and RSUs to new executive officer hires.

Under the terms of our 2023 Plan, pursuant to which all equity grants are currently made, the exercise price of any stock options awarded must be equal to at least 100% of the fair market value of our common stock (the closing sales price on The Nasdaq Global Select Market) on the date of grant.

Authority to make equity grants to executive officers rests with the Compensation Committee. Recommendations for equity grants are made by Aon based on grant values for similarly situated executive positions in our peer group companies and accounting for dilution constraints and management of our burn rate. Our CEO recommends grants for individual executives within those guidelines. The Compensation Committee then reviews and considers our CEO's recommendation and approves the final grant amounts. The Compensation Committee also determines and approves the final grant amounts to our CEO.

We believe that annual equity awards serve as a useful performance recognition mechanism, encouraging the retention of executive officers by maintaining their focus on our long-term performance, as well as on the achievement of specific performance goals. Our typical option awards to executive officers (including our named executive officers) have a term of 10 years and vest and become exercisable over a period of four years, with 25% of the underlying shares vesting on the first anniversary of the grant date and the remainder monthly over the next three years. Our typical RSU awards to executive officers (including our named executive officers) vest and become exercisable over a period of four years, with 25% of the underlying shares vesting on each anniversary of the grant date.

In addition to the new hire and annual equity awards described above, the Compensation Committee considers grants of other equity awards, as needed, to align business strategy with our compensation practices.

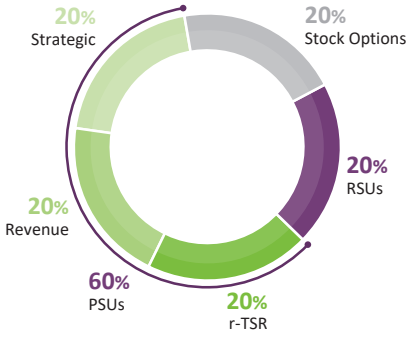
Annual Equity Grants in Fiscal 2024

Grants of Ultragenyx Awards

In March 2024, the Compensation Committee approved equity grants that reflected an equal value split among options, RSUs and PSUs for our named executive officers other than our Chief Executive Officer, who instead received 60% of his grant in the form of PSUs,

with the remaining portion split equally among options and RSUs. The increased portion of our Chief Executive Officer's annual equity grant that is performance-based is intended to enhance the alignment with stockholder interests.

2024 CEO Annual Equity Awards Mix



The PSU awards granted to our executive officers in March 2024 (2024 PSUs) consist of a revenue portion (1/3 of the 2024 PSUs, which reflects a decrease from 50% of the 2023 PSUs) with a two-year performance period, a relative TSR portion (1/3 of the 2024 PSUs, which reflects an increase compared to 25% of the 2023 PSUs) with a three-year performance period and a strategic performance portion (1/3 of the 2024 PSUs, which reflects an increase compared to 25% of the 2023 PSUs) with a three-year performance period, which is longer than the two-year performance period for the strategic portion of the 2023 PSUs. The increased emphasis on relative TSR portion and the strategic performance portion of the PSU awards reduces the overall portion of our incentive compensation program that is focused on revenue and creates a more balanced mix of performance goals that are key to creation of long-term success. The increased performance period for the strategic performance portion of the 2024 PSUs results in additional program rigor due to a sustained performance requirement over a longer timeframe.

The revenue-based 2024 PSUs will vest based upon achievement of revenue-based targets during the period beginning January 1, 2024 and ending December 31, 2025, with all of the earned revenue-based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2026. The revenue-based PSUs will be earned at 50% of target for threshold performance and 200% of target for maximum performance, with no PSUs being earned for below threshold performance.

The relative TSR-based 2024 PSUs will vest based upon our TSR performance relative to the TSR of the companies in the Nasdaq Biotechnology Index during the period beginning January 1, 2024 and ending December 31, 2026, with all of the earned relative TSR-based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2027. The relative TSR-based PSUs will be earned as follows based on our percentile ranking among the Nasdaq Biotechnology Index during the performance period:

Level of Performance	TSR Percentile	Earned TSR PSUs
Threshold	25th	25%
Target	50th	100%
Stretch	75th	150%
Maximum	90th	200%

The strategic performance based 2024 PSUs will vest upon achievement of specified strategic performance objectives during the period between January 1, 2024 and ending December 31, 2026, with all of the earned strategic performance based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2027. The strategic performance based PSUs will be earned as follows based on the number of strategic goals achieved during the performance period. No PSUs are earned under the strategic performance based 2024 PSUs for below threshold performance.

Level of Performance	Number of Strategic Goals Achieved	Earned Strategic 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%

The tables below set forth all equity awards granted in fiscal 2024 to our named executive officers.

Name	Date of Grant	Number of Options	Number of RSUs	Target Number of PSUs
Emil D. Kakkis, M.D., Ph.D.	3/1/2024	70,094	38,428	115,284
Howard Horn	3/1/2024	34,200	19,400	19,400
Erik Harris	3/1/2024	34,200	19,400	19,400
Eric Crombez, M.D.	3/1/2024	34,200	19,400	19,400
John R. Pinion II	3/1/2024	31,400	17,800	17,800

Grants of Performance Stock Options (PSOs) in Amlogenyx Inc. (Amlogenyx)

In addition to grants of Ultragenyx options, RSUs and PSUs in fiscal 2024 as described above, in recognition of their contributions to Amlogenyx, Dr. Kakkis, Mr. Horn and Mr. Pinion also received grants of PSOs from Amlogenyx, a privately-held subsidiary of Ultragenyx in which Ultragenyx currently holds a majority interest, during fiscal 2024. The Amlogenyx PSOs will vest upon achievement of specified performance criteria related to clinical milestones, with each criteria weighted 25%. If the performance criteria are not achieved by the end of the 18 month performance period on April 21, 2026, the unvested portion of the Amlogenyx PSOs will be forfeited.

Name	Date of Grant	Number of Amlogenyx PSOs
Emil D. Kakkis, M.D., Ph.D.	10/21/2024	350,000
Howard Horn	10/21/2024	22,500
John R. Pinion II	10/21/2024	100,000

Performance of 2023 PSUs

The PSU awards granted to our executive officers in March 2023 (2023 PSUs) consisted of a revenue portion with a two-year performance period (50% of the PSUs), a relative TSR portion (25% of the PSUs) with a three-year performance period and a strategic performance portion (25% of the PSUs) with a two-year performance period. The performance periods of the revenue portion and strategic performance portion of the 2023 PSUs ended on December 31, 2024 and the revenue portion and strategic performance portion of the 2023 PSUs vested on March 1, 2025, as described below. The performance period for the relative TSR-based 2023 PSUs extends through December 31, 2025, and if earned, such portion will vest in early 2026.

Achievement of Revenue Portion of 2023 PSUs

The revenue-based 2023 PSUs vested based upon achievement of the following revenue-based targets (and application of linear interpolation) during the period beginning January 1, 2023 and ending December 31, 2024, with all of the earned revenue-based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2025.

Level of Performance	Aggregate Revenue	Earned Revenue-Based PSU Percentage
Threshold	$ 945M	50%
Actual	**$ 995M**	**74%**
Target	$ 1,050M	100%
Maximum	$ 1,260M	200%

In February 2025, based on the Company's 2023 and 2024 revenue performance measured in accordance with U.S. GAAP (GAAP), the Compensation Committee certified that the revenue based 2023 PSUs were earned at 74% of target, and such earned 2023 PSUs vested on March 1, 2025.

Achievement of Strategic Performance Portion of 2023 PSUs

The strategic performance based 2023 PSUs vested upon achievement of specified strategic performance objectives during the period between January 1, 2023 and ending December 31, 2024, with all of the earned strategic performance based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2025.

Level of Performance	Number of Strategic Goals Achieved	Earned Strategic PSUs
Threshold	2 out of 5	50%
Target	3 out of 5	100%
Actual	**3.5 out of 5**	**125%**
Stretch	4 out of 5	150%
Maximum	5 out of 5	200%

In February 2025, based on the Company's achievement of 3.5 out of 5 strategic performance objectives, the Compensation Committee certified that the strategic performance portion of 2023 PSUs were earned at 125% of target, and such earned 2023 PSUs vested on March 1, 2025.

Performance of 2022 PSUs

The PSU awards granted to our executive officers in March 2022 (2022 PSUs) consisted of a revenue portion with a two-year performance period (80% of the PSUs) and a relative TSR portion with a three-year performance period (20% of the PSUs). In February 2024, based on the Company's 2022 and 2023 revenue performance measured in accordance with GAAP, the Compensation Committee certified that the threshold level of revenue-based 2022 PSUs had not been achieved and as a result, the revenue-based portion of the 2022 PSUs were forfeited.

The relative TSR-based 2022 PSUs vested based upon our TSR performance relative to the TSR of the companies in the Nasdaq Biotechnology Index during the period beginning January 1, 2022 and ending December 31, 2024, with all of the earned relative TSR-based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2025. The relative TSR-based PSUs was earned as follows based on our percentile ranking among the Nasdaq Biotechnology Index during the performance period:

Level of Performance	TSR Percentile	Earned TSR PSUs
Threshold	25th	25%
Target	50th	100%
Actual	**62nd**	**124%**
Stretch	75th	150%
Maximum	90th	200%

Based on the Company's ranking relative to the TSR of the companies in the Nasdaq Biotechnology Index of the 62nd percentile during the performance period, in February 2025, the Compensation Committee certified that the relative TSR-based 2022 PSUs were earned at 124% of target, and such earned 2022 PSUs vested on March 1, 2025.

Fiscal 2025 Compensation

Peer Group

The Compensation Committee reviews our list of peer companies annually to determine if revisions are needed to reflect changes in our development status, market capitalization, changes in individual peer companies, and other factors. The Compensation Committee engaged Aon to assist in reviewing our peer group and in suggesting revisions, as appropriate.

Based on Aon's assessment and recommendations, the Compensation Committee selected 20 publicly traded companies in the pharmaceutical and biotechnology industries to serve as our new list of peer companies for 2025, referred to as our 2025 peer group, by balancing the following criteria:

- companies with emphasis on orphan pharmaceutical products;
- companies with comparable market capitalizations (i.e., in the range of $2 billion to $14 billion);
- companies with revenue of between $250 million and $1.6 billion; and
- companies with headcounts between 300 to 4,000 employees.

Our 2025 peer group is comprised of the following 19 companies in the pharmaceutical and biotechnology industries, reflecting the addition of Axsome Therapeutics, Inc., Denali Therapeutics Inc. and Vericel Corporation and the removal of BioCryst Biopharmaceuticals, Inc., FibroGen, Inc. and Sage Therapeutics, Inc. from our 2024 peer group due to misalignment with our market capitalization and the removal of BioMarin Biopharmaceutical Inc. who exceeded our market capitalization and revenue ranges.

ACADIA Pharmaceuticals Inc.	Corcept Therapeutics Inc.	Jazz Pharmaceuticals plc
Alkermes plc	Denali Therapeutics Inc.	Neurocrine Biosciences, Inc.
Amicus Therapeutics	Exelixis Inc.	PTC Therapeutics, Inc.
Apellis Pharmaceuticals, Inc.	Halozyme Therapeutics	Sarepta Therapeutics, Inc.
Axsome Therapeutics, Inc.	Insmed Incorporated	Vericel Corporation
Blueprint Medicines Corporation	Intra-Cellular Therapies Inc.	
BridgeBio Pharma, Inc.	Ionis Pharmaceuticals, Inc.	

We believe that the compensation practices of our 2025 peer group provided us with appropriate compensation benchmarks for evaluating the compensation of our named executive officers for 2025.

Base Salaries

For 2025, increases in base salaries for our named executive officers, were 5.1% annualized for Dr. Crombez to align to the external market peer group, 2.9% annualized for Mr. Horn, 2.5% annualized for Mr. Harris and 2.8% annualized for Mr. Pinion. Dr. Kakkis opted not to receive an increase to his base salary for 2025. The overall 2025 merit budget was based on an Aon trend report regarding projected market merit budgets and spend for 2025.

Annual Bonuses

For 2025, the Compensation Committee maintained the target annual bonus of 80% for our Chief Executive Officer and maintained the target bonus amount of 50% for all other named executive officers. No significant changes were made to the bonus plan for 2025.

Equity Compensation

For 2025, the Compensation Committee determined to increase the PSU component of the annual equity grants to our executive officers, other than our Chief Executive Officer, from 33% to 50%, with the remaining portion of the grant equally split at 25% options and 25% RSUs. For our Chief Executive Officer, the Compensation Committee maintained the equity split of 60% PSUs, 20% options and 20% RSUs.

The PSU awards granted to our executive officers in 2025 (2025 PSUs) consist of a revenue portion with a two-year performance period (1/3 of the 2025 PSUs), a relative TSR portion with a three-year performance period (1/3 of PSUs) and a strategic performance portion (1/3 of the PSUs) with a three-year performance period. The revenue-based 2025 PSUs will vest based upon achievement of revenue-based targets during the period beginning January 1, 2025 and ending December 31, 2026, with all of the earned revenue-based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2027. The relative TSR-based 2025 PSU awards will vest based upon our TSR performance relative to the TSR of the companies in the Nasdaq Biotechnology Index during the period beginning January 1, 2025 and ending December 31, 2027, with a maximum payout of 100% of target in the event our absolute TSR is negative, with all of the earned relative TSR-based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2028. The strategic-based 2025 PSU awards will vest based on achievement of specified strategic goals during the period beginning January 1, 2025 and ending December 31, 2027, with all of the earned strategic based PSUs vesting on the later of (i) the date in which the Compensation Committee certifies such achievement and (ii) March 1, 2028. The PSUs will be earned at 50% of target for threshold performance (or 25% of target for the relative TSR-based PSUs) and 200% of target for maximum performance, with no PSUs becoming earning for below threshold performance.

Employee Benefits Program

Executive officers are eligible to participate in all of our employee benefit plans, including medical, dental, vision, group life, disability, and accidental death and dismemberment insurance. In each case, participation is on the same basis as other employees, subject to applicable law. We also provide vacation and other paid holidays to all employees, including executive officers, all of which we believe to be comparable to those provided at peer companies. These benefit programs are designed to enable us to attract and retain our workforce in a competitive marketplace. Reliable and competitive health, welfare and vacation benefits ensure that we have a productive and focused workforce.

In addition, our named executive officers are eligible to participate in a retirement savings plan (401(k) Plan), which is a tax-qualified defined contribution plan pursuant that allows participants to contribute certain amounts of their annual compensation, subject to limits prescribed by the Internal Revenue Service. All of our employees are eligible to participate in the 401(k) Plan on the same terms as the named executive officers.

Our named executive officers, along with our other highly-compensated U.S. based employees and non-employee directors of our Board, are also eligible to participate in our nonqualified deferred compensation plan. Please see ” -Nonqualified Deferred Compensation Plan” below for a summary of the plan.

Clawback Policy

Our Board has adopted a Clawback Policy intended to comply with the listing standards from Nasdaq implementing Exchange Act Rule 10D-1. In the event the Company is required to prepare an accounting restatement of the Company’s financial statements due to material non-compliance with any financial reporting requirement under the federal securities laws, the Company will recover, on a reasonably prompt basis, the excess incentive-based compensation received by any covered executive officer, including the named executive officers, during the prior three fiscal years that exceeds the amount that the named executive officer otherwise would have received had the incentive-based compensation been determined based on the restated financial statements. The Clawback Policy also permits recoupment of all incentive compensation, including time-based and performance-based equity awards and bonuses, in the event of fraud or intentional misconduct by a current or former executive officer, including the named executive officers.

Minimum Stock Ownership Requirements

We maintain stock ownership guidelines in order to align the long-term interests of our executive officers and directors with those of our stockholders. The guidelines require holding shares of our common stock with value equivalent to 3x the annual retainer for Board members, 3x base salary for our Chief Executive Officer and 1x base salary for the other named executive officers. Shares that count toward satisfaction of these guidelines include shares owned outright by the individual (including RSUs that have vested), shares

retained after an option exercise or issuance under another type of equity award granted under the Company's equity incentive plans, shares retained after purchase under the ESPP and shares held in trust for the benefit of the individual. Unexercised options and unvested and unearned RSUs and PSUs do not count towards satisfaction of these guidelines. These guidelines were required to be achieved by the end of 2022 for our named executive officers and Board members who have been named executive officers and Board members as of the date the policy was implemented and within five years of appointment for newly appointed named executive officers and Board members. As of December 31, 2024, each of our Board members and named executive officers who were required to be in compliance with the guidelines by the end of 2024 had met the ownership guidelines.

Equity Grant Timing

Generally, the Compensation Committee grants annual equity awards, including stock options, on March 1 of each year following the filing of our Annual Report on Form 10-K and grants new hire equity awards, including stock options, on the 16th of each month following the individual's start date. The Compensation Committee may also grant equity awards at other times during the year, such as in connection with special retention awards, performance recognition, or in the event of a significant change in job responsibilities. Under the 2014 Employee Stock Purchase Plan, eligible employees may purchase shares at a discount, with purchase dates generally on April 30 and October 31 of each yar, using payroll deductions accumulated during the prior six-month period. The Compensation Committee did not take material nonpublic information into account when determining the timing and terms of equity awards, including stock options, during 2024, and we did not time the disclosure of material nonpublic information for the purpose of affecting the value of executive compensation. During 2024, no stock options were granted to the named executive officers in the period beginning four business days before and ending one business day after the filing or furnishing of any Form 10-Q, Form 10-K or Form 8-K that disclosed material nonpublic information.

Risk Management and Mitigation

In reviewing the compensation structure in fiscal 2024, the Compensation Committee also considered how our compensation policies may affect our risk profile and how compensation policies may be used to mitigate risks facing us. More specifically, the Compensation Committee considered the general design philosophy of our policies for employees whose conduct would be most affected by incentives established by compensation policies. In considering these issues, the Compensation Committee concluded that the use of performance-based bonuses and long-term equity awards did not appear to create undue risks for us or encourage excessive risk-taking behavior on the part of employees.

With respect to bonus awards, the amount of an individual's award depends principally (exclusively, in the case of our Chief Executive Officer) on our overall performance, which reduces the ability and incentive for an individual to take undue risks in an effort to increase the amount of his or her bonus award for a particular year. For fiscal 2024, our corporate goals were reviewed and approved by the Board in early 2024, upon the recommendation of the Compensation Committee, and are considered to be generally of the nature that would not encourage or reward excessive risk taking. Additionally, the Compensation Committee monitors our performance throughout the year and has the ability to intervene in instances where our actions vis-à-vis our performance goal attainment would be considered unduly risky, so that the Compensation Committee may act to prevent or penalize such actions.

With respect to equity awards, these awards typically vest over several years, meaning that long-term value creation, contrasted with short-term gain, presents the best opportunity for employees to benefit from these awards.

Compensation Committee Report

The Compensation Committee has reviewed and discussed with management the Compensation Discussion and Analysis required by Item 402(b) of Regulation S-K. Based on this review and discussion, the Compensation Committee recommended to the Board of Directors that the foregoing Compensation Discussion and Analysis be included in this Proxy Statement and incorporated by reference in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024.

Submitted by the Compensation Committee of the Board of Directors

Michael Narachi, Chairman
Deborah Dunsire, M.D.
Daniel G. Welch

Summary Compensation Table

The following table sets forth the compensation earned during the years ended December 31, 2024, 2023, and 2022 by our Chief Executive Officer, our Chief Financial Officer and our next three highest-paid executives. We refer to these officers as our named executive officers.

Name and Principal Position	Year	Salary	Bonus	Stock Award[1]	Option Award[2]	Non-Equity Incentive Plan Compensation[3]	All Other Compensation[4]	Total
Emil D. Kakkis, M.D., Ph.D. President and Chief Executive Officer	2024	$ 856,008	$ —	$ 9,374,511	$ 2,715,600	$ 757,768	$ 13,800	$ 13,717,687
	2023	823,692	—	9,456,663	2,161,782	622,656	13,200	13,077,993
	2022	796,154	—	7,463,295	3,310,681	558,000	12,200	12,140,330
Howard Horn Chief Financial Officer, Corporate Strategy and Executive Vice President	2024	590,000	—	2,271,944	1,076,335	343,970	13,800	4,296,049
	2023	124,808	60,000	2,867,459	2,888,773	—	—	5,941,040
Erik Harris Chief Commercial Officer and Executive Vice President	2024	604,231	—	2,271,944	1,038,603	367,235	13,800	4,295,813
	2023	585,969	—	2,169,750	1,020,050	279,598	13,200	4,068,567
	2022	566,331	—	2,007,768	892,550	269,706	12,200	3,748,555
Eric Crombez, M.D. Chief Medical Officer and Executive Vice President	2024	591,846	—	2,271,944	1,038,603	382,030	13,800	4,298,223
John R. Pinion II Chief Quality Officer and Executive Vice President, Translational Sciences	2024	570,366	—	2,084,548	1,121,271	339,768	13,800	4,129,753
	2023	552,092	—	2,169,750	1,020,050	294,761	13,200	4,049,853
	2022	533,315	—	2,007,768	892,550	260,678	12,200	3,706,511

(1) The amounts reported in this column for a fiscal year represent the grant date fair value of the RSUs and PSUs granted to our named executive officers during the fiscal year, as computed in accordance with ASC Topic 718, not including any estimates of forfeitures, and, with respect to the PSUs, assuming the most probable outcome of the performance conditions as of the grant date. The assumptions used in calculating the grant date fair value of the RSUs and PSUs reported in this column are set forth in the notes to our financial statements included in our Annual Report. The amounts reported in this column reflect the accounting cost for these RSUs and PSUs and do not correspond to the actual economic value that may be realized by the named executive officers from the RSUs and the PSUs. The value of the PSUs reported in this column for 2024, assuming achievement of the maximum performance level, was as follows: $14,622,623 for Dr. Kakkis, $2,460,715 for each of Mr. Horn, Dr. Crombez and Mr. Harris and $2,257,733 for Mr. Pinion.

(2) The amounts reported in this column for a fiscal year represent the grant date fair value of the stock options granted to our named executive officers during the fiscal year, as computed in accordance with ASC Topic 718, not including any estimates of forfeitures. Amounts included in this column for Dr. Kakkis, Mr. Horn and Mr. Pinion also include the grant date fair value of the PSOs granted from Amlogenyx, a privately-held subsidiary of Ultragenyx in which Ultragenyx currently holds a majority interest, as described above under " *—Annual Equity Grants in Fiscal 2024*". The grant date fair value of the Amlogenyx PSOs is as follows: $586,950 for Dr. Kakkis, $37,733 for Mr. Horn and $167,700 for Mr. Pinion. The assumptions used in calculating the grant date fair value of the Amlogenyx PSOs reported in this column were as follows: expected term of 5.75 years, risk free rate of 3.98%, volatility of 85% and exercise price of $2.31. The amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the named executive officers from the options.

(3) Amounts for a fiscal year represent annual cash bonuses earned in that fiscal year and paid in the subsequent fiscal year based on achievement of performance goals and other factors deemed relevant by our Compensation Committee under our annual incentive program.

(4) Amounts reported in this column for the 2024 fiscal year reflects 401(k) matching contributions.

Narrative Disclosure to Summary Compensation Table

Employment Arrangements with Our Named Executive Officers

Dr. Kakkis, our Chief Executive Officer, is party to an employment agreement with us that provides for base salary and participation in our employee benefit plans, subject to the terms of those plans. Pursuant to the terms of the employment agreement, the employment of Dr. Kakkis is at will; we may terminate his employment at any time, without advance notice, for any reason or for no reason at all, and Dr. Kakkis may terminate his employment at any time, upon four weeks' prior written notice, for any reason or for no reason at all.

Each of our other named executive officers is party to an offer letter with us that provides for base salary, an annual bonus opportunity, and an initial grant of equity. They are eligible to participate in our employee benefit plans, subject to the terms of those plans. Pursuant to the terms of the offer letters, their employment is at will and may be terminated either by us or by them, with or without advance notice, for any reason or for no reason at all. Pursuant to Mr. Horn's offer letter, he received a $60,000 sign-on bonus in 2023, which was subject to repayment in the event his employment is terminated for "cause" (as defined below) or as a result of his resignation that is not a "constructive termination" (as defined below) within 12 months of his start date, which obligation lapsed in 2024.

Each of these employment arrangements and offer letters, as amended, also contain provisions that provide for certain payments and benefits in the event of an involuntary termination of employment. In addition, the named executive officers may be entitled to accelerated vesting of their outstanding and unvested awards in certain circumstances. The information below describes certain compensation that may become due and payable as a result of certain events as reflected in the amended arrangements.

Involuntary Termination of Employment

Pursuant to their employment arrangements or offer letters, each named executive officer is eligible to receive certain payments and benefits in the event of certain qualifying terminations, including termination of his or her employment by us without "cause" (as defined below) or resignation of his or her employment with "good reason" or because of a "constructive termination" (each, as defined below). Certain benefits are enhanced in the event the qualifying termination occurs within a specified period of time (12 months for Dr. Kakkis, and 18 months for Mr. Horn, Mr. Harris, Dr. Crombez and Mr. Pinion) after the consummation of a "covered transaction" (as defined below), which we refer to as the covered transaction protection period. Upon the timely execution of a general release of claims, each named executive officer is eligible to receive the following payments and benefits:

- if Dr. Kakkis is terminated by us other than for cause (and not as a result of death or disability) or he resigns for good reason, he will be entitled to receive (i) the sum of 24 months of his base salary and his target bonus for the year in which the termination occurs (or, if such termination occurs within the covered transaction protection period, the sum of 24 months of his base salary and 2x his target bonus), (ii) reimbursement for monthly COBRA premiums for the 24-month period following his termination, (iii) if such termination occurs within the covered transaction protection period, accelerated vesting of any unvested equity-based compensation; and
- if Mr. Horn, Mr. Harris, Dr. Crombez or Mr. Pinion is terminated by us without cause (and not as a result of death or disability) or upon a resignation due to a constructive termination, the executive will be entitled to the following severance benefits: (i) extension of the exercise period applicable to any options to purchase our stock held by the executive at the time of termination until 12 months from the date of such termination (or, if earlier, until the expiration of the term of the option set forth in the applicable option award agreement), (ii) the sum of 12 months of the executive's base salary and the executive's target bonus for the year in which the termination occurs (or, if such termination occurs within the covered transaction period, the sum of 18 months of the executive's base salary and 1.5x the executive's target bonus), (iii) reimbursement for monthly COBRA premiums for the 12-month period following the executive's termination (or, if such termination occurs within the covered transaction protection period, for the 18-month period following the executive's termination), (iv) if such termination occurs within the covered transaction period, accelerated vesting of any unvested equity-based compensation, and (v) if such termination occurs within the covered transaction period, extension of the exercise period applicable to any outstanding options held by the executive until 12 months from the date of such termination (or, if earlier, until the expiration of the term of the option set forth in the applicable option award agreement).

Definitions

For purposes of Dr. Kakkis' employment agreement, "cause" means his:

- commission of a felony or any crime involving dishonesty, breach of trust, or physical harm to any person;
- willful engagement in conduct that is in bad faith and materially injurious to us, including but not limited to misappropriation of trade secrets, fraud, or embezzlement;
- material breach of his employment agreement that is not cured within 10 days after written notice to him from us; or
- willful refusal to implement or follow a lawful policy or directive of ours, which breach is not cured within 10 days after written notice to him from us.

For purposes of each of the offer letters with Mr. Horn, Mr. Harris, Dr. Crombez and Mr. Pinion "cause" means the named executive officer's:

- willful engagement in conduct that is materially injurious to the Company (for Mr. Harris) or gross negligence in carrying out, or material failure to carry out, his or her duties for us (including, without limitation, failure to cooperate in any Company investigation), after notice from the Board and a reasonable opportunity to cure (if deemed curable);
- breach of his or her fiduciary duties to us, after notice from the Board and a reasonable opportunity to cure (if deemed curable);
- conviction of, or plea of guilty or no contest to, any felony;
- act of fraud or embezzlement with respect to his or her obligations to us or otherwise relating to our business;
- willful refusal to implement or follow a material policy or directive (for Mr. Horn, Dr. Crombez and Mr. Harris) or a material violation of any of our policies (for Mr. Pinion), in each case other than for Mr. Pinion and Dr. Crombez after notice from the Board and a reasonable opportunity to cure (if deemed curable);
- material breach of any agreement entered into with us (subject to notice from the Board and a reasonable opportunity to cure (if deemed curable) for Mr. Horn); or
- unauthorized use or disclosure of confidential information or trade secrets of ours or of our affiliates (subject to notice from the Board and a reasonable opportunity to cure (if deemed curable) for Mr. Horn).

For purposes of Dr. Kakkis' employment agreement, "good reason" means any of the following events without his consent, subject to standard notice and cure requirements:

- a change in his position with us that materially reduces his level of responsibility;
- a material reduction in his base salary, except for reductions that are comparable to reductions generally applicable to similarly situated executives of ours; or
- a relocation of his principal place of employment by more than 50 miles.

For purposes of each of the offer letters with Mr. Horn, Mr. Harris, Dr. Crombez and Mr. Pinion, "constructive termination" means the occurrence of any of the following events without the named executive officer's consent, subject to standard notice and cure requirements:

- a material reduction or change in the executive's job duties, responsibilities and requirements from the executive's job duties, responsibilities and requirements immediately prior to such reduction or change, taking into account the differences in job title and duties that are normally occasioned by reason of an acquisition of one company by another;
- a material reduction of the executive's base salary (other than an equal, across-the-board reduction in the compensation of all similarly-situated employees of ours or the surviving entity that is approved by the Board); or
- a requirement that the executive relocate to a principal office that increases his or her one-way commute by more than 50 miles relative to the executive's immediately preceding principal office.

Grants of Plan-Based Awards

The following table sets forth certain information regarding grants of plan-based awards to the named executive officers during fiscal 2024.

		Estimated Future Payouts Under Non-Equity Incentive Plan Awards[1]			Estimated Future Payouts Under Equity Incentive Plan Awards[2]			Stock Awards: Number of Shares of Stock or Units Granted (#)[3]	Option Awards: Number of Securities Underlying Options Granted (#)	Exercise Price of Option Awards ($/Share)	Grant Date Fair Value of Stock and Option Awards ($)[4]
Name	**Grant Date**	**Threshold ($)**	**Target ($)**	**Maximum ($)**	**Threshold (#)**	**Target (#)**	**Maximum (#)**				
Emil D. Kakkis, M.D., Ph.D.		344,400	688,800	1,033,200	—	—	—	—	—	—	—
	3/1/2024	—	—	—	—	—	—	—	70,094	53.69	2,128,650
	3/1/2024	—	—	—	—	—	—	38,428	—	—	2,063,199
	3/1/2024	—	—	—	48,045	115,284	230,568	—	—	—	7,311,311
	10/21/2024[5]	—	—	—	—	350,000	—	—	—	2.31	586,950
Howard Horn		—	295,000	588,525	—	—	—	—	—	—	—
	3/1/2024	—	—	—	—	—	—	—	34,200	53.69	1,038,603
	3/1/2024	—	—	—	—	—	—	19,400	—	—	1,041,586
	3/1/2024	—	—	—	8,085	19,400	38,800	—	—	—	1,230,358
	10/21/2024[5]	—	—	—	—	22,500	—	—	—	2.31	37,733
Erik Harris		—	303,500	605,483	—	—	—	—	—	—	—
	3/1/2024	—	—	—	—	—	—	—	34,200	53.69	1,038,603
	3/1/2024	—	—	—	—	—	—	19,400	—	—	1,041,586
	3/1/2024	—	—	—	8,085	19,400	38,800	—	—	—	1,230,358
Eric Crombez., M.D.		—	302,000	602,490	—	—	—	—	—	—	—
	3/1/2024	—	—	—	—	—	—	—	34,200	53.69	1,038,603
	3/1/2024	—	—	—	—	—	—	19,400	—	—	1,041,586
	3/1/2024	—	—	—	8,085	19,400	38,800	—	—	—	1,230,358
John R. Pinion II		—	286,000	570,570	—	—	—	—	—	—	—
	3/1/2024	—	—	—	—	—	—	—	31,400	53.69	953,571
	3/1/2024	—	—	—	—	—	—	17,800	—	—	955,682
	3/1/2024	—	—	—	7,418	17,800	35,600	—	—	—	1,128,866
	10/21/2024[5]	—	—	—	—	100,000	—	—	—	2.31	167,700

(1) The amounts in these columns represent the threshold (for Dr. Kakkis only), target and maximum amount of each named executive officer's cash payments under our 2024 annual incentive program as established by the Board and described in "Compensation Discussion and Analysis" above. Actual payments made for fiscal 2024 are provided in the Summary Compensation Table.

(2) The amounts in these columns represent the threshold, target and maximum level of achievement for the 2024 PSUs granted under our 2023 Incentive Plan. The PSU awards consist of a revenue portion (33.4% of the PSUs) with a two-year performance period, a relative total stockholder return (TSR) portion (33.3% of the PSUs) with a three-year performance period and a strategic performance portion (33.3% of the PSUs) with a three-year performance period. See "—Annual Equity Grants in Fiscal 2024" above for a description of the 2024 PSUs.

(3) The amounts in this column represents the RSUs granted under our 2023 Plan during 2024.

(4) This column reflects the aggregate grant date fair value of equity awards granted in 2024 as computed in accordance with ASC Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock and option awards reported in this column are set forth in Note 13 to our financial statements included in our Annual Report for fiscal 2024.

(5) Reflects PSOs granted by Amlogenyx, a privately-held subsidiary of Ultragenyx in which Ultragenyx currently holds a majority interest, as described above under "*—Annual Equity Grants in Fiscal 2024*". The Amlogenyx PSOs will vest upon achievement of specified clinical performance criteria, with each criteria weighted 25%. If the performance criteria are not achieved during the 18-month performance period ending April 21, 2026, any unvested portion of the Amlogenyx PSOs will be forfeited.

Outstanding Equity Awards at December 31, 2024

The following table sets forth information concerning the outstanding equity awards held by each of the named executive officers as of December 31, 2024.

		Option Awards[1]					Stock Awards			
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)[2]	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)[3]	Market Value of Shares or Units of Stock That Have Not Vested ($)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)[4]	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested ($)
Emil D. Kakkis, M.D., Ph.D.	10/21/2024	—	—	350,000	2.31	10/21/2034	—	—	—	—
	3/1/2024	—	70,094	—	53.69	3/1/2034	38,428	1,616,666	115,284	4,849,998
	3/1/2023	36,531	46,969	—	45.65	3/1/2033	129,036	5,428,545	44,314	1,864,290
	3/1/2022	63,498	28,862	—	67.37	3/1/2032	38,926	1,637,617	—	—
	3/1/2021	33,750	2,250	—	142.47	3/1/2031	4,500	189,315	—	—
	3/1/2020	56,100	—	—	56.08	3/1/2030	—	—	—	—
	3/1/2019	66,000	—	—	67.55	3/1/2029	—	—	—	—
	3/1/2018	94,500	—	—	48.43	3/1/2028	—	—	—	—
	3/1/2017	78,000	—	—	88.80	3/1/2027	—	—	—	—
	6/1/2016	63,700	—	—	70.57	6/1/2026	—	—	—	—
	5/21/2015	68,300	—	—	84.89	5/21/2025	—	—	—	—
Howard Horn	10/21/2024	—	—	22,500	2.31	10/21/2034	—	—	—	—
	3/1/2024	—	34,200	—	53.69	3/1/2034	19,400	816,158	19,400	816,158
	10/9/2023	40,971	99,498	—	35.68	10/9/2033	60,274	2,535,727	—	—
Erik Harris	3/1/2024	—	34,200	—	53.69	3/1/2034	19,400	816,158	19,400	816,158
	3/1/2023	17,238	22,162	—	45.65	3/1/2033	31,471	1,323,985	7,029	295,710
	3/1/2022	17,119	7,781	—	67.37	3/1/2032	10,472	440,557	—	—
	3/1/2021	10,313	687	—	142.47	3/1/2031	1,375	57,846	—	—
	3/1/2020	22,000	—	—	56.08	3/1/2030	—	—	—	—
	6/19/2019	12,000	—	—	63.27	6/19/2029	—	—	—	—
	3/1/2019	13,000	—	—	67.55	3/1/2029	—	—	—	—
	3/1/2018	3,900	—	—	48.43	3/1/2028	—	—	—	—
	7/6/2017	30,000	—	—	63.28	7/6/2027	—	—	—	—
Eric Crombez, M.D.	3/1/2024	—	34,200	—	53.69	3/1/2034	19,400	816,158	19,400	816,158
	5/1/2023	3,310	5,052	—	44.03	5/1/2033	18,464	776,780	7,029	295,710
	3/1/2023	4,308	5,537	—	45.65	3/1/2033	5,538	232,984	—	—
	3/1/2022	7,491	8,249	—	67.37	3/1/2032	1,587	66,765	—	—
	4/16/2021	—	—	—	—		500	21,035	—	—
	3/1/2021	4,041	269	—	142.47	3/1/2031	360	15,145	—	—
	3/1/2020	13,000	—	—	56.08	3/1/2030	—	—	—	—
	3/1/2019	8,000	—	—	67.55	3/1/2029	—	—	—	—
	11/17/2017	7,500	—		48.11	11/17/2027	—	—	—	—

		Option Awards[1]					Stock Awards			
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)[2]	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)[3]	Market Value of Shares or Units of Stock That Have Not Vested ($)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)[4]	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested ($)
John R. Pinion II	10/21/2024	—	—	100,000	2.31	10/21/2034	—	—	—	—
	3/1/2024	—	31,400	—	53.69	3/1/2034	17,800	748,846	17,800	748,846
	3/1/2023	17,238	22,162	—	45.65	3/1/2033	31,471	1,323,985	7,029	295,710
	3/1/2022	17,119	7,781	—	67.37	3/1/2032	10,472	440,557	—	—
	3/1/2021	10,313	687	—	142.47	3/1/2031	1,375	57,846	—	—
	3/1/2020	22,000	—	—	56.08	3/1/2030	—	—	—	—
	3/1/2019	23,000	—	—	67.55	3/1/2029	—	—	—	—
	3/1/2018	27,000	—	—	48.43	3/1/2028	—	—	—	—
	3/1/2017	18,000	—	—	88.80	3/1/2027	—	—	—	—
	6/3/2016	11,000	—	—	69.53	6/3/2026	—	—	—	—
	6/1/2016	17,800	—	—	70.57	6/1/2026	—	—	—	—
	7/16/2015	90,000	—	—	124.87	7/16/2025	—	—	—	—

(1) The options vest with respect to 1/4th of the shares underlying the option on the one-year anniversary of the applicable grant date, and with respect to 1/48th of the shares underlying the option, on each monthly anniversary thereafter, subject to the holder's continued service to us through each such vesting date. Please see the section entitled "—Narrative Disclosure to Summary Compensation Table—Covered Transaction" for accelerated vesting provisions that apply on certain terminations of employment.

(2) Reflects PSOs from Amlogenyx, a privately-held subsidiary of Ultragenyx in which Ultragenyx currently holds a majority interest. The Amlogenyx PSOs will vest upon achievement of specified clinical performance criteria, with each criteria weighted 25%. If the performance criteria are not achieved during the 18-month performance period ending April 21, 2026, any unvested portion of the Amlogenyx PSOs will be forfeited.

(3) Amounts in this column reflects unvested RSUs as well as earned but unvested PSUs. The RSUs vest with respect to 1/4th of the underlying shares on each anniversary of the grant date over a four-year period. For (i) Dr. Kakkis, 12,906 of the total earned PSUs listed in the March 1, 2022 row and 94,386 of the total earned PSUs listed in the March 1, 2023 row vested on March 1, 2025 and for (ii) each of Mr. Harris and Mr. Pinion, 3,472 of the total earned PSUs listed in the March 1, 2022 row, for Mr. Harris and Mr. Pinion, 14,971 of the total earned PSUs listed in the March 1, 2023 row vested on March 1, 2025 and for Dr. Crombez, 14,971 of the of the total earned PSUs listed in the May 1, 2023 row vested on March 1, 2025. Please see the section entitled "—Narrative Disclosure to Summary Compensation Table—Covered Transaction" for accelerated vesting provisions that apply on certain terminations of employment.

(4) The PSUs set forth in the table are reported at target achievement. The PSUs vest as described above under "Compensation Discussion and Analysis—Equity Compensation". Please see the section entitled "—Narrative Disclosure to Summary Compensation Table—Covered Transaction" for accelerated vesting provisions that apply on certain terminations of employment.

Option Exercises and Stock Vested

The following table sets forth certain information concerning the stock awards vested for our named executive officers during fiscal 2024. No named executive officers exercised any option awards during fiscal 2024.

	Stock Awards	
Name	Number of Shares Acquired on Vesting (#)	Value Realized on Vesting ($)[1]
Emil D. Kakkis, M.D., Ph.D.	36,442	1,956,571
Howard Horn	20,092	1,072,511
Erik Harris	13,282	713,111
Eric Crombez, M.D.	5,781	292,588
John R. Pinion II	11,620	623,878

(1) Value realized is equal to the closing price of our common stock on The Nasdaq Global Select Market on each vesting date multiplied by the number of shares of stock that vested on such date.

Pension Benefits

We do not have a defined benefit plan. Our named executive officers did not participate in, or otherwise receive any special benefits under, any pension or defined benefit retirement plan sponsored by us during fiscal 2024.

Nonqualified Deferred Compensation

In June 2021, we adopted a non-qualified deferred compensation plan (Deferred Compensation Plan). Our Deferred Compensation Plan permits highly-compensated U.S. based employees, including our named executive officers, as well as non-employee members of the Board to defer up to 75% of their base salary and up to 100% of director compensation and other types of compensation, including annual cash bonuses, RSUs and PSUs awarded.

Generally, a deferral election must be made no later than December 31 of the previous year and is irrevocable. Deferrals with respect to salary are deducted from the participant's salary in equal installments for the period of January 1 to December 31 of each year. These deferral elections are for the salary earned by the participant for the particular salary pay period during that year, which would otherwise be payable to the participant in such pay period. The election to defer salary under the Deferred Compensation Plan is in addition to any deferral election made by the participant under our 401(k) Plan. Deferrals for performance-based annual bonuses are for those bonuses earned during the year for which the election applies, which are payable the following year. The Deferred Compensation Plan is intended to provide participants with a tax deferral opportunity for compensation paid by us. The deferred amounts are not subject to income tax or income tax withholding when earned and deferred, but are fully taxable (and withheld appropriately) when distributed.

The Deferred Compensation Plan authorizes the Company to make matching contributions at our sole discretion. The participant is 100% vested at all times in his or her deferred cash account (including any company matching contributions), and deferrals of any compensation subject to vesting (such as RSUs and PSUs) shall vest in accordance with the provisions of the underlying award. No matching contributions were made by the Company in 2024.

The Deferred Compensation Plan provides for distribution of deferred compensation and earnings thereon upon a participant's separation from service with us, his or her retirement, a date specified by the participant in his or her compensation deferral agreement, the death of a participant (in such a case, to the designated beneficiary) or a "change in control." Payment distributions can be made in a lump sum, annual installments of up to five years at the participant's election or for "specified date accounts only", installments of up to 15 years, at the participant's election.

The Deferred Compensation Plan credits gains and losses to deferred amounts based upon "deemed" investments in mutual funds investing in equity instruments or debt securities chosen by each participant (which the participant may change at any time) from a "menu" of fund options provided by us. The investment returns credited to participants' accounts in the Deferred Compensation Plan correspond to actual returns of the chosen funds. The performance of the mutual funds fluctuates with the conditions of the capital markets and the economy generally, and is affected by prevailing interest rates and credit risks. The investment options under the Deferred Compensation Plan include:

Fund	2024 Rate of Return (%)
PIMCO VIT Short-Term Admin	6.1
Vanguard VIF Total Bond Market Index	1.2
Western Asset Core Plus Vit I	(0.4)
DFA VIT Inflation-Protected Secs Instl.	1.9
Empower Multi-Sector Bond Investor (MXLMX)	5.1
American Funds IS® Capital World Bond 2	(3.0)
Vanguard VIF Equity Income	15.1
Fidelity® VIP Index 500 Initial	24.9
Invesco VI Equally Wtd S&P 500 I	12.7
T. Rowe Price Blue Chip Growth Port	35.5
American Century Vp Mid Cap Value I (AVIPX)	8.7
Empower S&P Mid Cap 400® Index Inv (MXMDX)	13.3
MFS® VIT Mid Cap Growth Init	14.7
Dimensional VA US Targeted Value	8.1
Empower S&P Smallcap 600® Index Inv (MXISX)	7.9
Clearbridge Variable Small Cap Growth I (QLMSIX)	4.5
Vanguard VIF Total Intl Stock Market Index	5.1
Vanguard VIF International	9.0
American Funds IS® New World 2	6.6
MFS® VIT III Global Real Estate Initial	(2.7)

For fiscal year 2024, other than Mr. Pinion, none of our named executive officers, participated in the Deferred Compensation Plan.

Name	Executive Contributions in Last FY ($)	Company Contributions in Last FY ($)	Aggregate Earnings in Last FY ($)	Aggregate Withdrawals/ Distributions ($)	Aggregate Balance at Last FYE ($)
Emil D. Kakkis, M.D., Ph.D., President and Chief Executive Officer	—	—	—	—	—
Howard Horn Chief Financial Officer, Corporate Strategy and Executive Vice President	—	—	—	—	—
Erik Harris, Chief Commercial Officer and Executive Vice President	—	—	—	—	—
Eric Crombez, M.D., Chief Medical Officer and Executive Vice President	—	—	—	—	—
John R. Pinion II, Chief Quality Officer and Executive Vice President, Translational Sciences	86,011[1]	—	29,798	—	333,174

(1) Represents the value of 1,602 RSUs as of the applicable vesting date that were deferred into the Deferred Compensation Plan upon the partial vesting of such RSUs.

Potential Payments Upon Termination or Change of Control

The amount of compensation and benefits payable to each named executive officer in various termination and change in control situations, as described above under "—Narrative Disclosure to Summary Compensation Table—Involuntary Termination of Employment" and "—Narrative Disclosure to Summary Compensation Table—Covered Transaction, has been estimated in the tables below. The tables below do not include the values of any amounts that a named executive officer may receive under the Deferred Plan as a result of a termination of employment or a change in control, as all amounts under the Deferred Plan are fully vested benefits.

The value of the option, RSU, and PSU vesting acceleration was calculated for each of the tables below based on the assumption that the change in control and executive's employment termination occurred on December 31, 2024. The closing price of our common stock on The Nasdaq Global Select Market as of December 31, 2024 was $42.07, which was used as the value of our common stock for purposes of the following tables. The value of the option vesting acceleration was calculated by multiplying the number of unvested option shares subject to vesting acceleration as of December 31, 2024 by the difference between the closing price of our common stock as of December 31, 2024 and the exercise price for such unvested option shares. No value is attributed to unvested options subject to acceleration which have exercise prices above the closing market price of our common stock as of December 31, 2024. The value of the RSU and PSU vesting acceleration was calculated by multiplying the number of unvested RSUs, earned but unvested PSUs and unearned PSUs (based on an assumed target level of performance) subject to vesting acceleration as of December 31, 2024 by the closing price of our common stock as of the last trading day of 2023. The value of COBRA reimbursements was calculated for each of the tables below based on the elections for each named executive officer in effect in December 2024 and the applicable COBRA premiums for December 2024.

Dr. Emil Kakkis

The following table describes the potential payments upon employment termination for Emil Kakkis, our President and Chief Executive Officer, as if his employment terminated as of December 31, 2024, the last business day of the fiscal year. Qualifying termination includes a termination by the Company without cause or a resignation by Dr. Kakkis for good reason.

Potential Payments Upon Termination or Change of Control	Qualifying Termination	Qualifying Termination following a Covered Transaction
Base Salary	$ 1,722,000	$ 1,722,000
Bonus	688,800	1,377,600
Acceleration of equity awards	—	15,586,430
COBRA reimbursements	40,086	40,086
TOTAL	**$ 2,450,886**	**$ 18,726,116**

Howard Horn

The following table describes the potential payments upon employment termination for Howard Horn, our Chief Financial Officer, Corporate Strategy and Executive Vice President, as if his employment terminated as of December 31, 2024, the last business day of the fiscal year. Qualifying termination includes a termination by the Company without cause or a resignation by Mr. Horn due to a constructive termination.

Potential Payments Upon Termination or Change of Control	Qualifying Termination	Qualifying Termination following a Covered Transaction
Base Salary	$ 590,000	$ 885,000
Bonus	295,000	442,500
Acceleration of equity awards	—	4,803,835
COBRA reimbursements	26,378	39,567
TOTAL	**$ 911,378**	**$ 6,170,902**

Erik Harris

The following table describes the potential payments upon employment termination for Erik Harris, our Chief Commercial Officer and Executive Vice President as if his employment terminated as of December 31, 2024, the last business day of the fiscal year. Qualifying termination includes a termination by the Company without cause or a resignation by Mr. Harris due to a constructive termination.

Potential Payments Upon Termination or Change of Control	Qualifying Termination	Qualifying Termination following a Covered Transaction
Base Salary	$ 607,000	$ 910,500
Bonus	303,500	455,250
Acceleration of equity awards	—	3,750,414
COBRA reimbursements	8,935	13,402
TOTAL	**$ 919,435**	**$ 5,129,566**

Eric Crombez, M.D.

The following table describes the potential payments upon employment termination for Eric Crombez, M.D., our Chief Medical Officer and Executive Vice President, as if his employment terminated as of December 31, 2024, the last business day of the fiscal year. Qualifying termination includes a termination by the Company without cause or a resignation by Mr. Pinion due to a constructive termination.

Potential Payments Upon Termination or Change of Control	Qualifying Termination	Qualifying Termination following a Covered Transaction
Base Salary	$ 604,000	$ 906,000
Bonus	302,000	453,000
Acceleration of equity awards	—	3,040,735
COBRA reimbursements	20,043	30,064
TOTAL	**$ 926,043**	**$ 4,429,799**

John R. Pinion II

The following table describes the potential payments upon employment termination for John Pinion, our Chief Quality Officer and Executive Vice President, Translational Sciences as if his employment terminated as of December 31, 2024, the last business day of the fiscal year. Qualifying termination includes a termination by the Company without cause or a resignation by Mr. Pinion due to a constructive termination.

Potential Payments Upon Termination or Change of Control	Qualifying Termination	Qualifying Termination following a Covered Transaction
Base Salary	$ 572,000	$ 858,000
Bonus	286,000	429,000
Acceleration of equity awards	—	3,615,790
COBRA reimbursements	39,974	59,961
TOTAL	**$ 897,974**	**$ 4,962,751**

Equity Compensation Plan Information

The table below discloses information as of December 31, 2024 with respect to our equity compensation plans that have been approved by stockholders and equity compensation plans that have not been approved by stockholders.

Plan Category	Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights(a)[1]	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance under Equity Compensation Plans (Excluding Securities Reflected in Column(a))
Equity compensation plans approved by security holders:			
2014 Incentive Plan	11,190,128	$68.34	—
2014 Employee Stock Purchase Plan	—	—	6,409,256
2023 Equity Incentive Plan	4,327,714	$52.87	6,139,766
Equity compensation plans not approved by security holders			
Dimension Therapeutics, Inc. 2015 Stock Option and Incentive Plan[2]	21,531	$49.12	—
Dimension Therapeutics, Inc. 2013 Stock Plan[2]	940	$28.66	—
Employment Inducement Plan	854,219	$47.66	211,628
TOTAL	**16,394,532**	**$65.75**	**12,760,650**

(1) Amounts in this column include outstanding stock options, RSUs and PSUs (assuming target performance for any unearned PSUs.

(2) In connection with our acquisition of Dimension Therapeutics, Inc. on November 7, 2017, we assumed these plans and outstanding option awards thereunder (whether or not then vested or exercisable). The assumed awards continue to have, and are subject to, the same terms and conditions as were applicable prior to the acquisition as set forth in the applicable plan (including any applicable award agreement, other agreement or other document evidencing such awards), except that the awards are exercisable for shares of our common stock with exercise prices adjusted to reflect the terms of the acquisition, all as set forth in the merger agreement. No new awards can be made under these plans.

Director Compensation

Our Board has adopted a non-employee director compensation policy that is designed to provide a total compensation package that enables us to attract and retain, on a long-term basis, high caliber non-employee directors. A Board compensation review prepared by Aon in February 2024 provided a competitive assessment of our compensation practices for non-employee directors in connection with the Compensation Committee's evaluation of the level of compensation for our non-employee directors for 2024.

A summary of the non-employee director cash compensation arrangements for fiscal 2024 is set forth below:

	Annual Retainer
Board of Directors:	
Chairman	$ 85,000
Non-Chairman members	$ 50,000
Audit Committee:	
Chairman	$ 25,000
Non-Chairman members	$ 12,500
Compensation Committee:	
Chairman	$ 20,000
Non-Chairman members	$ 10,000
Nominating and Corporate Governance Committee:	
Chairman	$ 12,000
Non-Chairman members	$ 6,000
Research and Development Committee:	
Chairman	$ 15,000
Non-Chairman members	$ 7,500

In 2025, upon recommendation of the Compensation Committee, the Board maintained the annual cash compensation levels under the non-employee director compensation policy.

Under the non-employee director compensation policy for fiscal 2024, each non-employee director who was initially appointed or elected to the Board received an equity award with a target value of $600,000, comprised 50% of options to purchase shares of our common stock and 50% of RSUs on the date he or she first becomes a non-employee director. The options vest monthly over a three-year period and the RSUs vest annually in equal amounts over a three-year period, in each case subject to the director's continued service to us through each such vesting date. In addition, for fiscal year 2024, on the date of the annual meeting of stockholders, each continuing non-employee director received an annual equity award at a target value of $400,000, comprised of 50% options to purchase shares of our common stock and 50% RSUs, each of which would vest in full upon the earlier of (1) our subsequent annual meeting of stockholders and (2) the first anniversary of the date of grant, subject to the director's continued service to us through such vesting date. The exercise price of all of the foregoing options was equal to the fair market value of a share of our common stock on the date of grant.

In 2025, upon recommendation of the Compensation Committee, the Board maintained the target values of annual awards for non-employee directors and the target annual awards for newly appointed directors.

Dr. Kakkis, our President and Chief Executive Officer, receives no compensation for his service as a director.

The following table shows the compensation earned in fiscal 2024 by our non-employee directors.

Name	Fees Earned or Paid in Cash in Fiscal 2024	Stock Awards[1]	Option Awards[2]	Total
Daniel G. Welch	$ 100,750	$ 200,010	$ 199,374	$ 500,134
Deborah Dunsire, M.D.	67,375	200,010	199,374	466,759
Matthew K. Fust	80,750	200,010	199,374	480,134
Michael Narachi	82,500	200,010	199,374	481,884
Amrit Ray, M.D.	64,750	200,010	199,374	464,134
Corsee D. Sanders, Ph.D.	69,875	200,010	199,374	469,259
Shehnaaz Suliman, M.D.	68,875	200,010	199,374	468,259

(1) The amounts reported in this column for a fiscal year represent the grant date fair value of the RSUs granted to our non-employee directors during fiscal 2024, as computed in accordance with ASC Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the RSUs reported in this column are set forth in the notes to our financial statements included in our Annual Report. The amounts reported in this column reflect the accounting cost for these RSUs, and do not correspond to the actual economic value that may be received by the non-employee directors from the RSUs. As of December 31, 2024, each of our non-employee directors had 5,345 outstanding RSUs.

(2) The amounts reported in this column represent the grant date fair value of the stock options granted to our non-employee directors during fiscal 2024, as computed in accordance with ASC Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in the notes to our financial statements included in our Annual Report. The amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the non-employee directors from the options. As of December 31, 2024, our then non-employee directors had the following outstanding options: Mr. Welch – 74,130; Dr. Dunsire – 60,380; Mr. Fust – 56,630; Mr. Narachi – 74,130; Dr. Ray – 32,780; Dr. Sanders – 30,510; and Dr. Suliman – 56,630.

CEO Pay Ratio

We are required by SEC rules adopted under the Dodd-Frank Act to disclose the ratio of our median employee's annual total compensation to the annual total compensation of our principal executive officer. This disclosure provides a measure of the equitability of pay within our company. We believe our compensation philosophy and process yield an equitable result for all of our employees. For 2024, the annual total compensation for Dr. Emil Kakkis, our Chief Executive Officer and President, was $13,717,687 and for our median employee was $325,295, resulting in a pay ratio of 42:1.

In accordance with Item 402(u) of Regulation S-K, we identified the median employee by (i) aggregating for each applicable employee (A) base salary for 2024 on the calculation date, (B) the target bonus for 2024, and (C) the accounting value of any equity awards granted during 2024, and (ii) ranking this annual compensation measure for our employees from lowest to highest. This calculation encompasses individuals, excluding our CEO, employed by us on October 1, 2024, whether employed on a full-time, part-time, or seasonal basis. For any permanent employees who were only employed for part of the 2024 fiscal year, we annualized their compensation to present a more accurate representation of their comparative annual compensation. On October 1, 2024, we had 1,291 employees. The total compensation of our identified median employee using the same methodology we use for our named executive officers as set forth in the Summary Compensation Table.

The SEC's rules for identifying the median employee and calculating the pay ratio based on that employee's annual total compensation allow companies to adopt a variety of methodologies, to apply certain exclusions, and to make reasonable estimates and assumptions that reflect their employee populations and compensation practices. As a result, the pay ratio reported by other companies may not be comparable to the pay ratio reported above, as other companies have different employee populations and compensation practices and may utilize different methodologies, exclusions, estimates and assumptions in calculating their own pay ratios.

Pay versus Performance

As required by Section 953(a) of the Dodd-Frank Wall Street Reform and Consumer Protection Act, and Item 402(v) of Regulation S-K, we are providing the following information about the relationship between Compensation Actually Paid (CAP) and certain financial performance of the Company. For further information concerning the Company's pay for performance philosophy and how the Company's aligns executive compensation with the Company's performance, refer to "Executive Compensation – Compensation Discussion and Analysis."

Year	Summary Compensation Table Total for PEO[1]	Compensation Actually Paid to PEO[2]	Average Summary Compensation Table Total for Non-PEO NEOs[3]	Average Compensation Actually Paid to Non-PEO NEOs[4]	Value of Initial Fixed $100 Investment Based On: Total Shareholder Return[5]	Value of Initial Fixed $100 Investment Based On: Peer Group Total Shareholder Return[6]	Net Income (Loss) (in thousands)[7]	Revenue (in thousands)[8]
2024	$ 13,717,687	$ 8,186,261	$ 4,254,959	$ 2,790,240	$ 99	$ 114	$ (569,183)	$ 560,230
2023	$ 13,077,993	$ 11,293,489	$ 4,524,001	$ 4,829,669	$ 112	$ 115	$ (606,639)	$ 434,249
2022	$ 12,140,330	$ 3,311,432	$ 3,911,773	$ (175,590)	$ 108	$ 111	$ (707,421)	$ 363,329
2021	$ 9,522,738	$ (2,152,804)	$ 3,314,256	$ (1,211,638)	$ 197	$ 125	$ (454,025)	$ 351,406
2020	$ 5,144,220	$ 22,726,743	$ 2,706,102	$ 8,015,000	$ 324	$ 126	$ (186,566)	$ 271,030

(1) The dollar amounts reported are the amounts in the "Total" column of the Summary Compensation Table in each applicable year for Dr. Kakkis, who served as our Chief Executive Officer during 2020, 2021, 2022, 2023 and 2024.

(2) The dollar amounts reported represent the amount of CAP, as computed in accordance with SEC rules. The dollar amounts do not reflect the actual amount of compensation earned by or paid during the applicable year. In accordance with SEC rules, the following adjustments were made to total compensation to determine the CAP:

Compensation Actually Paid to PEO	2024	2023	2022	2021	2020
Summary Compensation Table Total	$ 13,717,687	$ 13,077,993	$ 12,140,330	$ 9,522,738	$ 5,144,220
Less, value of "Stock Awards" and "Option Awards" reported in Summary Compensation Table	(12,090,111)	(11,618,444)	(10,773,976)	(8,246,092)	(3,709,589)
Plus, year end fair value of outstanding and unvested equity awards granted during the year	8,562,675	11,288,072	(6,264,762)	4,152,033	10,163,438
Plus (less), change in fair value from prior year end to current year end of outstanding and unvested equity awards granted in prior years	(2,033,745)	(1,167,400)	(2,934,552)	(5,753,632)	9,346,926
Plus (less), change in fair value from prior year end to vesting date of equity awards granted in prior years that vested in the year	29,755	(286,732)	(1,385,132)	(1,827,851)	1,781,748
Less, prior year-end fair value of any equity awards that failed to meet vesting conditions in the year	—	—	—	—	—
Compensation Actually Paid to Dr. Kakkis	**$ 8,186,261**	**$ 11,293,489**	**$ 3,311,432**	**$ (2,152,804)**	**$ 22,726,743**

(3) The dollar amounts reported represent the average of the amounts reported for the Company's named executive officers (NEOs) as a group (excluding our CEO) in the "Total" column of the Summary Compensation Table in each applicable year. The names of each of the NEOs (excluding our CEO) included for purposes of calculating the average amounts in each applicable year are as follows: (i) for 2024, Mr. Horn, Erik Harris, Dr. Crombez and Mr. Pinion, (ii) for 2023, Mr. Horn, Mr. Harris, Mr. Pinion and Ms. Parschauer, (iii) for 2022 and 2021, Dr. Camille Bedrosian, Mr. Harris, Mr. Pinion and Mardi Dier; and (iv) for 2020, Dr. Bedrosian, Ms. Dier, Mr. Harris, Mr. Pinion, and Shalini Sharp.

(4) The dollar amounts reported represent the average amount of CAP to the NEOs as a group (excluding our CEO), as computed in accordance with SEC rules. The dollar amounts do not reflect the actual average amount of compensation earned by or paid to the NEOs as a group (excluding our CEO) during the applicable year. In accordance with the SEC rules, the following adjustments were made to average total compensation for the NEOs as a group (excluding our CEO) for each year to determine the compensation actually paid, using the same methodology described above in Note 2:

Compensation Actually Paid to Non-PEO NEOs	2024	2023	2022	2021	2020
Summary Compensation Table Total	$ 4,254,959	$ 4,524,001	$ 3,911,773	$ 3,314,256	$ 2,706,102
Less, value of "Stock Awards" and "Option Awards" reported in Summary Compensation Table	(3,293,798)	(3,831,408)	(3,130,468)	(2,519,639)	(2,027,088)
Plus, year end fair value of outstanding and unvested equity awards granted during the year	2,412,702	4,476,201	1,264,910	1,268,695	4,150,071
Plus (less), change in fair value from prior year end to current year end of outstanding and unvested equity awards granted in prior years	(607,133)	(237,537)	(784,234)	(2,359,539)	2,748,610
Plus (less), change in fair value from prior year end to vesting date of equity awards granted in prior years that vested in the year	23,510	(101,588)	(573,020)	(915,411)	437,305
Less, prior year-end fair value of any equity awards that failed to meet vesting conditions in the year	—	—	(864,551)	—	—
Compensation Actually Paid to Non-PEO NEOs	**$ 2,790,240**	**$ 4,829,669**	**$ (175,590)**	**$ (1,211,638)**	**$ 8,015,000**

(5) Cumulative TSR is calculated by dividing (a) the sum of (i) the cumulative amount of dividends for the measurement period, assuming dividend reinvestment, and (ii) the difference between the Company's share price at the end and the beginning of the measurement period by (b) the Company's share price at the beginning of the measurement period. The beginning of the measurement period for each year in the table is December 31, 2019.

(6) Represents the weighted peer group TSR, weighted according to the respective companies' stock market capitalization at the beginning of each period for which a return is indicated. The peer group used for this purpose is the following published industry index: Nasdaq Biotechnology Index.

(7) The dollar amounts reported represent the amount of net income calculated in accordance with GAAP reflected in the Company's audited financial statements for the applicable year.

(8) The dollar amounts reported represent the amount of revenue calculated in accordance with GAAP reflected in the Company's audited financial statements for the applicable year.

Performance Measures

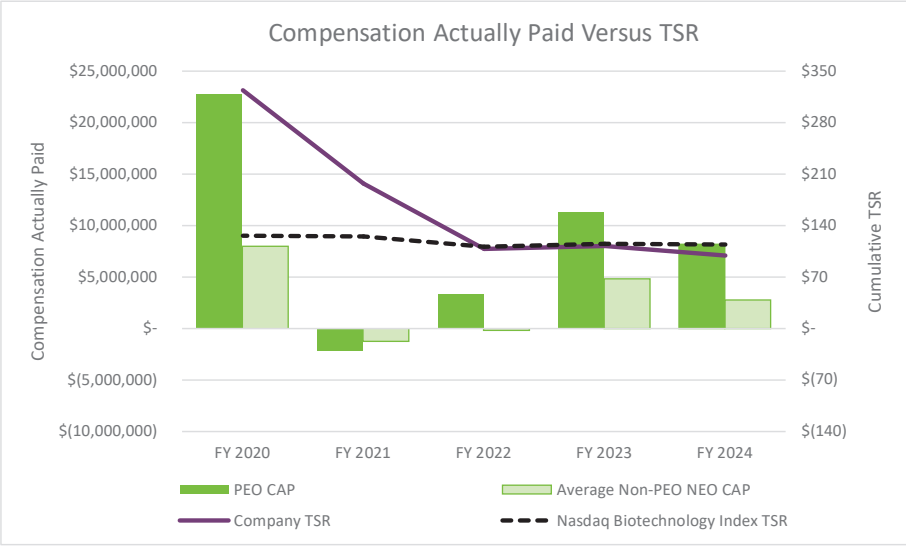
As described in greater detail in "Executive Compensation – Compensation Discussion and Analysis," the Company's executive compensation program reflects a variable pay-for-performance philosophy. The metrics that the Company uses for both our long-term and short-term incentive awards are selected based on an objective of incentivizing our NEOs to increase the value of our enterprise for our stockholders. The most important performance measures used by the Company to link executive compensation actually paid to the Company's NEOs, for the most recently completed fiscal year, to the Company's performance are as follows:

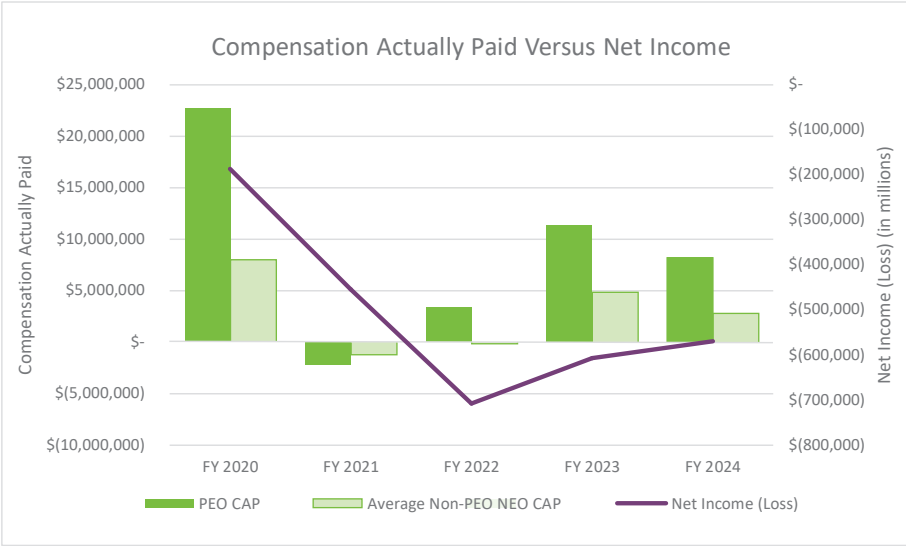
- Total Revenue
- Relative Total Stockholder Return
- Net Cash Used in Operations
- Clinical Development of Product Candidates

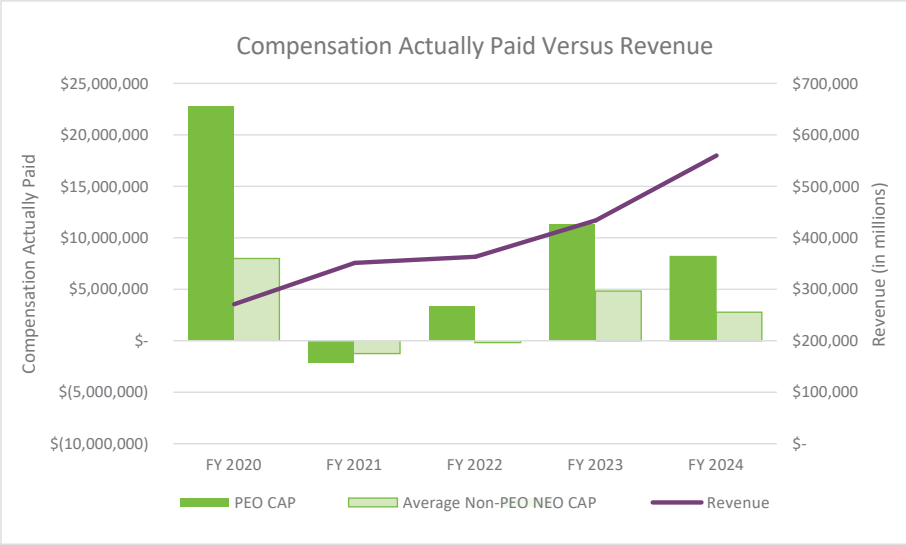
Description of the Relationship between Pay and Performance

As described in more detail in the section "Executive Compensation – Compensation Discussion and Analysis," the Company's executive compensation program reflects a variable pay-for-performance philosophy. While the Company utilizes several performance measures to align executive compensation with Company performance, all of those Company measures are not presented in the Pay versus Performance table. Moreover, the Company generally seeks to incentivize long-term performance, and therefore does not specifically align the Company's performance measures with compensation that is actually paid (as computed in accordance with SEC rules) for a particular year. In accordance with SEC rules, the Company is providing the following descriptions of the relationships between information presented in the Pay versus Performance table.

The following graphs provide visual representations of the relationship between both the CAP of our PEO and the average CAP of our non-PEO NEOs and our (i) TSR, (ii) net income, and (iii) Revenue.







Additional Information

Questions and Answers About these Proxy Materials and Voting

Why did I receive a one-page notice in the mail regarding the Internet availability of proxy materials instead of a full set of proxy materials?

Pursuant to rules adopted by the SEC, we have elected to provide access to our proxy materials over the Internet. Accordingly, we are sending an Important Notice Regarding the Availability of Proxy Materials (the Notice of Internet Availability) to our stockholders of record. All stockholders will have the ability to access the proxy materials on the website referred to in the Notice of Internet Availability free of charge or request to receive a printed set of the proxy materials for the Annual Meeting. Instructions on how to access the proxy materials over the Internet or to request a printed copy may be found in the Notice of Internet Availability.

We intend to mail the Notice of Internet Availability beginning on or about March 28, 2025 to all stockholders of record entitled to vote at the Annual Meeting.

What if I received more than one Notice of Internet Availability?

If you receive more than one Notice of Internet Availability, your shares may be registered in more than one name or are registered in different accounts. Please follow the voting instructions on each Notice of Internet Availability and cast your vote with respect to each set of proxy materials to ensure that all of your shares are voted.

When and where will the Annual Meeting be held?

The Annual Meeting will be held on May 15, 2025 at 9:00 a.m. Pacific Time virtually via the Internet at *www.virtualshareholdermeeting.com/RARE2025*. We conduct the Annual Meeting virtually via the Internet to facilitate stockholder attendance and participation and have done so every year since our initial public offering. We believe the virtual format for the Annual Meeting enhances stockholder access by allowing our stockholders to participate fully, and equally, from any location around the world at no cost. Taking advantage of this virtual approach reduces our expenses and eliminates the time we would otherwise spend managing the various aspects of holding a physical meeting. We believe the virtual format is the right choice for us, not only because it brings cost savings to us and our stockholders, but because it increases our ability to engage with all stockholders, regardless of size, resources, or physical location.

We are aware of concerns that virtual meetings may diminish stockholder voice or reduce accountability and have taken steps to address these concerns. For example, we believe that our virtual meeting format enhances, rather than constrains, stockholder access, participation, and communication because the online format allows stockholders to communicate with us during the Annual Meeting. Stockholders can ask questions of our Board, management, and a representative from our independent registered public accounting firm during the meeting. During the live Q&A session, we will answer questions as they come in, as time permits, and in accordance with the meeting rules of conduct that will be available at the virtual meeting website. Following the Annual Meeting, we intend to publish and answer any questions received that comply with the meeting of conduct and that are not answered at the meeting. Although the live webcast is available only to stockholders as of the Record Date (defined below) at the time of the Annual Meeting, the webcast of the Annual Meeting will be archived for the public for one year after the date of the Annual Meeting at *www.virtualshareholdermeeting.com/RARE2025*.

Our annual meetings are only one aspect of our stockholder outreach program, which is a year-long effort by our management to engage with our stockholders in a continuous and meaningful way. Our stockholders can raise questions or concerns regarding the Company at any time by calling our Investor Relations department at (844) 280-7681 or contacting our Board by following the process described under "Corporate Governance—Stockholder Communications".

To participate in the Annual Meeting, you must access the meeting website above, enter your 16-digit control number found on your Notice of Internet Availability, proxy card or voting instruction form, and follow the instructions on the website. If your shares are held in street name and your Notice of Internet Availability or voting instruction form indicates that you may vote those shares through *www.proxyvote.com,* then you may access, participate in and vote at the Annual Meeting with the 16-digit access code indicated on that Notice of Internet Availability or voting instruction form. Otherwise, stockholders who hold their shares in street name should contact their bank, broker or other nominee (preferably at least five days before the Annual Meeting) and obtain a "legal proxy" in order to be able to attend, participate in or vote at the Annual Meeting.

What am I voting on?

At the Annual Meeting, you will be asked to consider and vote upon:

1. The election of the two directors named in the Proxy Statement as Class III directors;
2. The approval of the Second A&R 2023 Plan;
3. The ratification of the selection of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2025; and
4. An advisory (non-binding) resolution to approve the compensation of our named executive officers.

What if another matter is properly brought before the Annual Meeting?

The Board of Directors is not aware of any other matter that will be presented for consideration at the Annual Meeting. If any other matters are properly brought before the Annual Meeting, the persons named in the accompanying proxy will vote on those matters in accordance with their best judgment.

What is the Board of Directors' voting recommendation?

The Board of Directors recommends that you vote your shares:

- **"FOR"** the election of each of the Class III director nominees;
- **"FOR"** the approval of the Second A&R 2023 Plan;
- **"FOR"** the ratification of the selection of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2025; and
- **"FOR"** the approval, on an advisory basis, of the compensation of our named executive officers

How many votes do I have?

Each share of common stock is entitled to one vote on all matters to be voted upon at the Annual Meeting. Holders of common stock do not have the right to cumulate votes in the election of directors.

When is the record date for the Annual Meeting?

The Board of Directors has fixed the close of business on March 24, 2025 as the record date for the Annual Meeting (Record Date).

How many shares must be represented in order to hold the Annual Meeting?

A quorum of stockholders is necessary to hold a valid stockholder meeting. A quorum will be present if stockholders holding at least a majority of the outstanding shares entitled to vote are present or represented by proxy at the Annual Meeting. On the Record Date, there were 93,899,667 shares outstanding and entitled to vote.

Your shares will be counted towards the quorum if you submit a valid proxy by mail, over the phone or via the Internet (or one is submitted on your behalf by your broker, bank or other nominee) or if you attend the Annual Meeting and vote. In addition, abstentions and broker non-votes will be counted towards the quorum requirement. If there is no quorum, the chair of the Annual Meeting may adjourn the meeting to another date.

How do I vote?

With regard to Proposal No. 1, the election of directors, you may vote "For" all the nominees to the Board or you may "Withhold" your vote for all the nominees or any individual nominee you specify. With regard to Proposals No. 2, 3 and 4 you may vote "For" or "Against" or abstain from voting.

The procedures for voting depend on whether your shares are registered in your name or are held by a bank, broker or other nominee:

Registered Holders: Shares Registered in Your Name

If you are a stockholder of record, you may vote at the Annual Meeting, which will be held virtually via the Internet, vote by proxy over the telephone, vote by proxy via the Internet, or vote by proxy using a proxy card that you may request or that we may elect to deliver at a later time. Whether or not you plan to attend the Annual Meeting, we urge you to vote by proxy to ensure your vote is counted. You may still attend the Annual Meeting and vote online even if you have already voted by proxy.

- To vote via the Internet, vote at www.proxyvote.com prior to 11:59 p.m. Eastern Time the day before the Annual Meeting.
- If you have received a paper copy of the proxy materials, vote over the telephone by calling 1-800-690-6903 prior to 11:59 p.m. Eastern Time the day before the Annual Meeting or by returning an executed proxy card (that we must receive before the Annual Meeting).
- Registered holders who attend the Annual Meeting may also vote during the Annual Meeting by going to www.virtualshareholdermeeting.com/RARE2024 and following the instructions regarding voting.

Beneficial Holders: Shares Registered in Name of Broker, Bank or Other Nominee

Persons who hold shares of Ultragenyx common stock indirectly on the Record Date through a brokerage firm, bank or other financial institution (beneficial holders) may vote before the Annual Meeting as follows:

- In accordance with the voting instructions provided by the institution that holds their shares, which may provide for voting over the telephone or via the Internet, or
- By returning a voting instruction form provided to them by the institution that holds their shares, in order to have their shares voted on their behalf.
- Beneficial holders who attend the Annual Meeting may also vote during the Annual Meeting by going to www.virtualshareholdermeeting.com/RARE2025 and following the instructions regarding voting.

What if I return a proxy card or otherwise vote but do not make specific choices?

If you are a stockholder of record and return a signed and dated proxy card or otherwise vote without marking voting selections, your shares will be voted in accordance with the Board's recommendations as describe under *"What is the Board of Directors' voting recommendation?"*. If any other matter is properly presented at the Annual Meeting, your proxy holder (one of the individuals named on your proxy card) will vote your shares in his or her discretion.

Are my shares voted if I do not provide a proxy or voting instructions?

If you are a stockholder of record and do not provide a proxy, you must attend the Annual Meeting in order to vote. If you hold shares through an account with a bank or broker and do not provide voting instructions, the bank or broker is permitted to vote your shares only on certain proposals considered "routine" matters. Whether a proposal is considered "routine" or "non-routine" is subject to stock exchange rules and final determination by the stock exchange. Even with respect to routine matters, some brokers are choosing not to exercise discretionary voting authority. Uninstructed shares that banks and brokers do not vote are counted as "broker non-votes." As a result, we urge you to direct your broker, fiduciary or custodian how to vote your shares to ensure that your interests are represented at the Annual Meeting.

What vote is required to approve each proposal and how are votes counted?

Proposal No. 1 — Election of directors

Directors are elected by a plurality of the votes cast, with the two nominees obtaining the greatest number of affirmative votes being elected as directors. Shares as to which a stockholder withholds voting authority and broker non-votes, if any, are not considered votes cast and therefore will have no effect on the vote outcome. As described above under "Proposal No. 1 – Election of Class III Directors," any nominee for director who receives a greater number of "withhold" votes for his or her election than votes "for" his or her election is expected to promptly tender his or her resignation to the Board following certification of the election results.

Each of the Other Proposals

Each of the other proposals must be approved by a majority of the votes cast on the proposal (meaning the number of shares voted "for" this proposal must exceed the number of shares voted "against" such proposal). As a result, abstentions and broker non-votes, if any, will have no effect on the vote outcome.

Can I change my vote after submitting my proxy?

Yes. If you are the registered holder of your shares, you may change or revoke a delivered proxy by:

- Executing and returning a new, later-dated proxy card by mail, or submitting a new vote via telephone or through the Internet, as instructed above in advance of the applicable deadline;
- Delivering a written revocation to the Corporate Secretary before the Annual Meeting; or
- Voting at the Annual Meeting. Simply attending the Annual Meeting will not, by itself, revoke or change your proxy.

If you hold your shares beneficially through a brokerage firm, bank or other financial institution, you should contact your brokerage firm, bank or other financial institution for information on how to change or revoke your proxy.

Who is paying for this proxy solicitation?

We are making these proxy materials available to you in connection with the solicitation of proxies by the Board of Directors of the Company. We will pay all of the costs of soliciting proxies. We will provide copies of our proxy materials to brokerage firms, fiduciaries, and custodians for forwarding to beneficial owners who request printed copies of these materials and will reimburse these persons for their costs of forwarding these materials. We have retained Innisfree, a proxy solicitation firm, for assistance in connection with the Annual Meeting at an estimated cost of up to approximately $25,000 plus reasonable out-of-pocket expense. Our directors, officers, and employees may also solicit proxies by telephone, facsimile, or personal solicitation; however, we will not pay these individuals additional compensation for any of these services.

When are stockholder proposals for inclusion in our proxy statement for next year's annual meeting due?

Stockholders wishing to present proposals for inclusion in our proxy statement for the 2026 Annual Meeting of Stockholder (2026 Annual Meeting) pursuant to Rule 14a-8 of the Exchange Act must submit their proposals so that they are received by us at our principal executive offices no later than the close of business (5:00 p.m. Pacific Time) on November 28, 2025. However, if our 2026 Annual Meeting is advanced or delayed by more than 30 days before or after the anniversary date of the 2024 annual meeting, then the deadline will be a reasonable time prior to the time that we begin to print and mail our proxy materials.

Proposals for inclusion in our proxy statement for the 2026 Annual Meeting should be sent to the Company's Corporate Secretary at 60 Leveroni Court, Novato, California 94949 and must satisfy the requirements of Rule 14a-8 of the Exchange Act. We reserve the right to exclude from our proxy statement any proposals not meeting such requirement.

When are other proposals and director nominations for next year's annual meeting due?

With respect to director nominations and proposals of other business (other than those to be included in our proxy statement pursuant to and in compliance with Rule 14a-8), our bylaws provide that stockholders who intend to present a stockholder proposal or director nomination at the 2026 Annual Meeting must deliver written notice of the proposal or nomination to our Corporate Secretary between 90 and 120 days prior to the one-year anniversary date of the Annual Meeting (that is, between January 15, 2026 and the close of business (5:00 p.m. Pacific Time) on February 14, 2026). If the 2026 Annual Meeting date is advanced by more than 30 days before or delayed by more than 60 days after the anniversary date of the Annual Meeting, then such notice must be received on or before the close of business (5:00 p.m. Pacific Time) on the later of 90th day before the date of the 2026 Annual Meeting or the 10th day after the day on which the date of the 2026 Annual Meeting is first disclosed in a public announcement. Notice of any such stockholder proposals and director nominations must satisfy the requirements set forth in our bylaws (which include timing and information required under Rule 14a-19 of the Exchange Act).

If a stockholder fails to meet these deadlines and fails to satisfy the requirements of Rule 14a-4 under the Exchange Act, we may exercise discretionary voting authority under proxies we solicit to vote on any such proposal as we determine appropriate. Proposals and nominations not meeting the requirements set forth in our bylaws will not be entertained at the Annual Meeting. All notices of proposals or nominations, as applicable, must be addressed to our Corporate Secretary at 60 Leveroni Court, Novato, California 94949. We reserve the right to reject, rule out of order, or take other appropriate action with respect to any nomination or proposal that does not comply with these and other applicable requirements.

How can I find out the result of the voting at the Annual Meeting?

Preliminary voting results will be announced at the Annual Meeting. In addition, final voting results will be published in a current report on Form 8-K that we expect to file with the SEC within four business days after the Annual Meeting.

Other Business

We know of no other matters to be submitted to a vote of stockholders at the Annual Meeting. In order for any stockholder to nominate a candidate or to submit a proposal for other business to be acted upon at a given annual meeting, he or she must provide timely written notice to our Corporate Secretary in the form prescribed by our bylaws, as described above.

Forward-Looking Statements

Certain of the statements made in this Proxy Statement are "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Exchange Act and the Private Securities Litigation Reform Act of 1995, including, among others, statements related to our expectations and projections regarding our future operating results and financial performance, anticipated cost or expense reductions, the timing, progress and plans for our clinical programs and clinical studies, future regulatory interactions, goals and other statements regarding our activities and initiatives covered in our Impact Report, anticipated effects of our executive compensation structure and programs, and the components and timing of regulatory submissions. Such forward-looking statements involve substantial risks and uncertainties that could cause our clinical development programs, collaboration with third parties, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, business and operating results, risks related to reliance on third party partners to conduct certain activities on the Company's behalf, uncertainty and potential delays related to clinical drug development, smaller than anticipated market opportunities for the Company's products and product candidates, manufacturing risks, competition from other therapies or products, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations, the Company's future operating results and financial performance, the timing of clinical trial activities and reporting results from same, and the availability or commercial potential of Ultragenyx's products and drug candidates. The Company expressly disclaims any obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of Ultragenyx in general, see our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 filed with the SEC in February 2025, and our subsequent annual and periodic reports filed with the SEC.

Delivery Of Proxy Materials

Our annual report to stockholders for the fiscal year ended December 31, 2024, including audited financial statements, accompanies this Proxy Statement. We will provide copies of our Annual Report without charge upon written request of a stockholder to our investor relations department at 60 Leveroni Court, Novato, California 94949. Copies of these materials are also available online through the SEC at *www.sec.gov.* We may satisfy SEC rules regarding delivery of proxy materials, including the Proxy Statement, Annual Report and Notice of Internet Availability by delivering a single copy of the proxy materials to stockholders who have the same address and do not participate in electronic delivery of proxy materials, a procedure adopted by the SEC called "householding." This delivery method can result in meaningful cost savings for us and conservation of natural resources. Under this procedure, only one copy of the proxy materials will be delivered to multiple stockholders who share an address, unless contrary instructions are received from one or more stockholders at that address. We undertake to deliver promptly upon written or oral request a separate copy of the Proxy statement, Annual Report or Notice of Internet Availability to a stockholder at a shared address to which a single copy of these materials was delivered. If you hold stock as a registered holder and prefer to receive separate copies of these materials either now or in the future, please contact our investor relations department at 60 Leveroni Court, Novato, California 94949 or by telephone at (415) 483-8800. Similarly, if you share an address with another stockholder and have received multiple copies of the proxy materials, you may write or call us at the address and phone number above to request delivery of a single copy of these materials in the future. If your stock is held through a brokerage firm, bank or other financial institution and you received a single copy of the proxy materials and prefer to receive separate copies of the proxy materials, either now or in the future, or if you received multiple copies of the proxy materials and prefer to receive a single copy in the future, please contact your brokerage firm, bank or other financial institution.

EACH STOCKHOLDER IS URGED TO VOTE VIA THE INTERNET AS INSTRUCTED IN THE NOTICE OF INTERNET AVAILABILITY OR, IF YOU REQUESTED AND RECEIVED A PRINTED COPY OF THE PROXY MATERIALS, BY COMPLETING, DATING, SIGNING AND RETURNING THE ENCLOSED PROXY CARD USING THE ENCLOSED RETURN ENVELOPE OR VOTING INSTRUCTION FORM PROVIDED WITH THE PRINTED PROXY MATERIALS, AS PROMPTLY AS POSSIBLE SO THAT YOUR SHARES MAY BE REPRESENTED AT THE ANNUAL MEETING.

APPENDIX A

Ultragenyx Pharmaceutical Inc. Second Amended and Restated 2023 Incentive Plan

1. Defined Terms

Exhibit A, which is incorporated by reference, defines the terms used in the Plan and sets forth certain operational rules related to those terms.

2. Purpose

The Plan has been established to advance the interests of the Company by providing for the grant to Participants of Stock-based and other incentive Awards. The Plan was originally approved by the Board on April 20, 2023 effective on the Original Effective Date and was amended and restated effective as June 18, 2024 and on May 15, 2025 (the "**Effective Date**").

3. Administration

The Administrator has discretionary authority, subject only to the express provisions of the Plan, to (a) interpret and construe the Plan, any rules and regulations under the Plan and the terms and conditions of any Award; (b) determine eligibility for and grant Awards; (c) determine, modify or waive the terms and conditions of any Award; (d) prescribe forms, rules and procedures relating to the Plan; (e) establish and verify the extent of satisfaction of any Performance Criteria or other conditions applicable to the grant, issuance, retention, vesting, exercisability or settlement of any Award; (f) determine the extent to which adjustments are required pursuant to Section 7; (g) approve corrections in the documentation or administration of any Award; and otherwise do all things necessary or appropriate to carry out the purposes of the Plan. Determinations of the Administrator made under the Plan will be conclusive and will bind all parties.

4. Limits on Awards Under the Plan

(a) Number of Shares.

(i) The maximum number of shares of Stock that may be delivered in satisfaction of Awards under the Plan is (A) 11,500,000, *plus* (B) the number of shares of Stock subject to any Award outstanding under a Prior Plan as of the Original Effective Date that after the Original Effective Date are not issued because such Award is forfeited, canceled, terminates, expires or otherwise lapses without being exercised (to the extent applicable), or is settled in cash. Up to 8,500,000 shares of Stock may be issued in satisfaction of ISOs, but nothing in this Section 4(a) will be construed as requiring that any, or any fixed number of, ISOs be awarded under the Plan. The limits set forth in this Section 4(a) shall be construed to comply with Section 422.

(ii) For purposes of this Section 4(a), if an outstanding Award is forfeited, canceled, terminates, expires or otherwise lapses without being exercised (to the extent applicable), or is settled in cash, the shares of Stock allocable to the terminated portion of such Award or such forfeited shares of Stock shall again be available for issuance under the Plan. Notwithstanding the foregoing, the following shares shall not be available for issuance under the Plan: (A) shares withheld from an Award under the Plan or a Prior Plan to satisfy the tax withholding obligations with respect to such Award, (B) shares withheld from an Award under the Plan or a Prior Plan in payment of the exercise price of an Award requiring exercise, (C) shares repurchased on the open market by the Company using proceeds from the exercise price paid with respect to Awards under the Plan or a Prior Plan, or (D) gross shares subject to an SAR granted under the Plan or a Prior Plan that are not issued in connection with the Stock-settlement of such SAR.

(b) Type of Shares. Stock delivered by the Company under the Plan may be authorized but unissued Stock or previously issued Stock acquired by the Company. No fractional shares of Stock will be delivered under the Plan.

(c) Limit on Non-Employee Director Compensation. The aggregate dollar value of equity-based (based on the grant date fair value of equity-based Awards determined for financial reporting purposes) and cash compensation granted under the Plan or otherwise to any non-employee director shall not exceed $900,000 during any calendar year for services provided as a non-employee director; provided, however, that in the calendar year in which a non-employee director first joins the Board or during any calendar year in which a non-employee director is designated as Chairman of the Board or Lead Director, the maximum aggregate dollar value of equity-based and cash compensation granted to the non-employee director may be up to $1,500,000.

5. Eligibility and Participation

The Administrator will select Participants from among key Employees and directors of, and consultants and advisors to, the Company and its Affiliates. Eligibility for ISOs is limited to individuals described in the first sentence of this Section 5 who are employees of the Company or of a "parent corporation" or "subsidiary corporation" of the Company as those terms are defined in Section 424 of the Code. Eligibility for Stock Options other than ISOs is limited to individuals described in the first sentence of this Section 5 who are providing direct services on the date of grant of the Stock Option to the Company or to a subsidiary of the Company that would be described in the first sentence of Section 1.409A-1(b)(5)(iii)(E) of the Treasury Regulations.

6. Rules Applicable to Awards

(a) All Awards.

(i) Award Provisions. The Administrator will determine the terms of all Awards, subject to the limitations provided herein. By accepting (or, under such rules as the Administrator may prescribe, being deemed to have accepted) an Award, the Participant will be deemed to have agreed to the terms of the Award and the Plan. Notwithstanding any provision of this Plan to the contrary, awards of an acquired company that are converted, replaced or adjusted in connection with the acquisition may contain terms and conditions that are inconsistent with the terms and conditions specified herein, as determined by the Administrator.

(ii) Term of Plan. No Awards may be made after 10 years from the Effective Date, but previously granted Awards may continue beyond that date in accordance with their terms. Notwithstanding the foregoing, no ISOs may be granted after 10 years from Date of Adoption.

(iii) Transferability. Neither ISOs nor, except as the Administrator otherwise expressly provides in accordance with the second sentence of this Section 6(a)(iii), other Awards may be transferred other than by will or by the laws of descent and distribution. During a Participant's lifetime, ISOs (and, except as the Administrator otherwise expressly provides in accordance with the second sentence of this Section 6(a)(iii), SARs and NSOs) may be exercised only by the Participant. The Administrator may permit the gratuitous transfer (i.e., transfer not for value) of Awards other than ISOs to any transferee eligible to be covered by the provisions of Form S-8 (under the Securities Act), subject to such limitations as the Administrator may impose.

(iv) Vesting, etc. The Administrator will determine the time or times at which an Award will vest or become exercisable and the terms on which a Stock Option or SAR will remain exercisable. Without limiting the foregoing, the Administrator may at any time accelerate the vesting or exercisability of an Award, regardless of any adverse or potentially adverse tax or other consequences resulting from such acceleration. Unless the Administrator expressly provides otherwise, however, the following rules will apply if a Participant's Employment ceases:

(A) Immediately upon the cessation of the Participant's Employment and except as provided in (B) and (C) below, each Stock Option and SAR that is then held by the Participant or by the Participant's permitted transferees, if any, will cease to be exercisable and will terminate and all other Awards that are then held by the Participant or by the Participant's permitted transferees, if any, to the extent not already vested will be forfeited.

(B) Subject to (C) and (D) below, all Stock Options and SARs held by the Participant or the Participant's permitted transferees, if any, immediately prior to the cessation of the Participant's Employment, to the extent then exercisable, will remain exercisable for the lesser of (i) a period of three months or (ii) the period ending on the latest date on which such Stock Option or SAR could have been exercised without regard to this Section 6(a)(iv), and will thereupon immediately terminate.

(C) All Stock Options and SARs held by a Participant or the Participant's permitted transferees, if any, immediately prior to the Participant's death, to the extent then exercisable, will remain exercisable for the lesser of (i) the one year period ending with the first anniversary of the Participant's death or (ii) the period ending on the latest date on which such Stock Option or SAR could have been exercised without regard to this Section 6(a)(iv), and will thereupon immediately terminate.

(D) All Stock Options and SARs (whether or not exercisable) held by a Participant or the Participant's permitted transferees, if any, immediately prior to the cessation of the Participant's Employment will immediately terminate upon such notice of cessation of Employment if the termination is for Cause or occurs in circumstances that in the sole determination of the Administrator would have constituted grounds for the Participant's Employment to be terminated for Cause.

(v) Additional Restrictions. The Administrator may cancel, rescind, withhold or otherwise limit or restrict any Award at any time if the Participant is not in compliance with all applicable provisions of the Award agreement and the Plan, or if the Participant breaches any agreement with the Company or its Affiliates with respect to confidentiality. Without limiting the generality of the foregoing, the Administrator may recover Awards made under the Plan and payments under or gain in respect of any Award to the extent required to comply with Company policy, including the Company's Clawback Policy.

(vi) Taxes. The delivery, vesting and retention of Stock, cash or other property under an Award are conditioned upon

full satisfaction by the Participant of all tax withholding requirements with respect to the Award. The Administrator will prescribe such rules for the withholding of taxes as it deems necessary. The Administrator may, but need not, hold back shares of Stock from an Award or permit a Participant to tender previously owned shares of Stock in satisfaction of tax withholding requirements (but not in excess of the maximum statutory withholding rate).

(vii) Dividend Equivalents, Etc. The Administrator may provide for the payment of amounts (on terms and subject to conditions established by the Administrator, except to the extent provided otherwise in this Section 6(a)(vii)) in lieu of cash dividends or other cash distributions with respect to Stock subject to an Award whether or not the holder of such Award is otherwise entitled to share in the actual dividend or distribution in respect of such Award. Any entitlement to dividend equivalents or similar entitlements will be established and administered either consistent with an exemption from, or in compliance with, the requirements of Section 409A. Dividends or dividend equivalent amounts payable in respect of Awards shall be subject to the same limits or restrictions as the Awards to which they relate and shall not be payable until such Awards vest. Notwithstanding the foregoing, no Stock Options or SARs shall provide for payment or accrual of dividends or dividend equivalents.

(viii) Rights Limited. Nothing in the Plan will be construed as giving any person the right to continued employment or service with the Company or its Affiliates, or any rights as a stockholder except as to shares of Stock actually issued under the Plan. The loss of existing or potential profit in Awards will not constitute an element of damages in the event of termination of Employment for any reason, even if the termination is in violation of an obligation of the Company or any Affiliate to the Participant.

(ix) Coordination with Other Plans. Awards under the Plan may be granted in tandem with, or in satisfaction of or substitution for, other Awards under the Plan or awards made under other compensatory plans or programs of the Company or its Affiliates. For example, but without limiting the generality of the foregoing, awards under other compensatory plans or programs of the Company or its Affiliates may be settled in Stock (including, without limitation, Unrestricted Stock) if the Administrator so determines, in which case the shares delivered will be treated as awarded under the Plan (and will reduce the number of shares thereafter available under the Plan in accordance with the rules set forth in Section 4).

(x) Section 409A. Each Award will contain such terms as the Administrator determines, and will be construed and administered, such that the Award either qualifies for an exemption from the requirements of Section 409A or satisfies such requirements.

(b) Stock Options and SARs.

(i) Time and Manner of Exercise. Unless the Administrator expressly provides otherwise, no Stock Option or SAR will be deemed to have been exercised until the Administrator receives a notice of exercise (in form acceptable to the Administrator), which may be an electronic notice, signed (including electronic signature in form acceptable to the Administrator) by the appropriate person and accompanied by any payment required under the Award. A Stock Option or SAR exercised by any person other than the Participant will not be deemed to have been exercised until the Administrator has received such evidence as it may require that the person exercising the Award has the right to do so.

(ii) Exercise Price. The exercise price (or the base value from which appreciation is to be measured) of each Award requiring exercise will be no less than 100% (or in the case of an ISO granted to a ten-percent shareholder within the meaning of Section 422, 110%) of the Fair Market Value of the Stock subject to the Award, determined as of the date of grant, or such higher amount as the Administrator may determine in connection with the grant.

(iii) Payment of Exercise Price. Where the exercise of an Award is to be accompanied by payment, payment of the exercise price will be by cash or check acceptable to the Administrator or by such other legally permissible means, if any, as may be acceptable to the Administrator.

(iv) Maximum Term. Stock Options and SARs will have a maximum term not to exceed 10 years from the date of grant (or five years from the date of grant in the case of an ISO granted to a ten-percent shareholder described in Section 6(b)(ii) above); provided, however, that, if a Participant still holding an outstanding but unexercised NSO or SAR 10 years from the date of grant (or, in the case of an NSO or SAR with a maximum term of less than 10 years, such maximum term) is prohibited by applicable law from exercising such Stock Options or SARs, and if at such time the Stock is publicly traded (as determined by the Administrator), the maximum term of such Award will instead be deemed to expire on the 30th day following the date the Participant is no longer prohibited from engaging in such open market sales.

(v) No Repricing without Stockholder Approval. The Company shall not, without stockholder approval (except in the case of a change in the Company's capitalization (as described in Section 7(b)), (A) reduce the exercise price of a Stock Option or SAR, (B) other than in the case of Covered Transaction, at any time when the exercise price of a Stock Option or SAR is above the Fair Market Value of a share of Stock, cancel and re-grant or exchange such Stock Option or SAR for cash or a new Award having a lower (or no) exercise price, or (c) take any other action with respect to an Award that would be treated as a repricing under generally accepted accounting principles.

(vi) No Reload Grants. Stock Options shall not be granted under the Plan in consideration for, and shall not be conditioned upon the delivery of, shares of Stock to the Company in payment of the exercise price and/or tax withholding obligation under any other employee stock option.

7. Effect of Certain Transactions

(a) Mergers, etc. Except as otherwise provided in an Award agreement, the following provisions will apply in the event of a Covered Transaction:

(i) Assumption or Substitution. If the Covered Transaction is one in which there is an acquiring or surviving entity, the Administrator may (but, for the avoidance of doubt, need not) provide (i) for the assumption or continuation of some or all outstanding Awards or any portion thereof or (ii) for the grant of new awards in substitution therefor by the acquiror or survivor or an affiliate of the acquiror or survivor. Notwithstanding any provision of this Section 7, in the event of a Covered Transaction in which the acquiring or surviving entity does not assume or continue outstanding Awards or provide for the grant of new awards in substitution therefor, all Awards that are not assumed, continued or substituted for shall be treated as follows effective immediately prior to the Covered Transaction: (A) in the case of a Stock Option or SAR, the Participant shall have the ability to exercise such Stock Option or SAR, including any portion of the Stock Option or SAR not previously exercisable, (B) in the case of any Award the vesting of which is in whole or in part subject to Performance Criteria, all conditions to the grant, issuance, retention, vesting or transferability of, or any other restrictions applicable to, such Award shall immediately lapse and the Participant shall have the right to receive a payment based on target level achievement or actual performance through a date determined by the Committee, as determined by the Committee, and (C) in the case of any other Award all conditions to the grant, issuance, retention, vesting or transferability of, or any other restrictions applicable to, such Award shall immediately lapse. In no event shall any action be taken pursuant to this Section 7(a)(i) that would change the payment or settlement date of an Award in a manner that would result in the imposition of any additional taxes or penalties pursuant to Section 409A of the Code.

(ii) Cash-Out of Awards. Subject to Section 7(a)(v) below the Administrator may (but, for the avoidance of doubt, need not) provide for payment (a "cash-out"), with respect to some or all Awards or any portion thereof, equal in the case of each affected Award or portion thereof to the excess, if any, of (A) the fair market value of one share of Stock (as determined by the Administrator in its reasonable discretion) times the number of shares of Stock subject to the Award or such portion, over (B) the aggregate exercise or purchase price, if any, under the Award or such portion (in the case of an SAR, the aggregate base value above which appreciation is measured), in each case on such payment terms (which need not be the same as the terms of payment to holders of Stock) and other terms, and subject to such conditions, as the Administrator determines; provided, however, that if the fair market value of one share of Stock (as determined by the Administrator in its reasonable discretion) does not exceed the exercise price of such Award, then the Award shall be cancelled without any payment of consideration therefor.

(iii) Acceleration of Certain Awards. Subject to Section 7(a)(v) below, the Administrator may (but, for the avoidance of doubt, need not) provide that any Award requiring exercise will become exercisable, in full or in part and/or that the delivery of any shares of Stock remaining deliverable under any outstanding Award of Stock Units (including Restricted Stock Units and Performance Awards to the extent consisting of Stock Units) will be accelerated in full or in part, in each case on a basis that gives the holder of the Award a reasonable opportunity, as determined by the Administrator, following exercise of the Award or the delivery of the shares, as the case may be, to participate as a stockholder in the Covered Transaction.

(iv) Termination of Awards Upon Consummation of Covered Transaction. Except as the Administrator may otherwise determine in any case, each Award will automatically terminate (and in the case of outstanding shares of Restricted Stock, will automatically be forfeited) upon consummation of the Covered Transaction, other than Awards assumed or continued pursuant to Section 7(a)(i) above.

(v) Additional Limitations. Any share of Stock and any cash or other property delivered pursuant to Section 7(a)(ii) or Section 7(a)(iii) above with respect to an Award may, in the discretion of the Administrator, contain such restrictions, if any, as the Administrator deems appropriate to reflect any Performance Criteria or other vesting conditions to which the Award was subject and that did not lapse (and were not satisfied) in connection with the Covered Transaction. For purposes of the immediately preceding sentence, a cash-out under Section 7(a)(ii) above or acceleration under Section 7(a)(iii) above will not, in and of itself, be treated as the lapsing (or satisfaction) of a Performance Criteria or other vesting condition. In the case of Restricted Stock that does not vest and is not forfeited in connection with the Covered Transaction, the Administrator may require that any amounts delivered, exchanged or otherwise paid in respect of such Stock in connection with the Covered Transaction be placed in escrow or otherwise made subject to such restrictions as the Administrator deems appropriate to carry out the intent of the Plan.

(b) Changes in and Distributions With Respect to Stock.

(i) Basic Adjustment Provisions. In the event of a stock dividend, stock split or combination of shares (including a reverse stock split), recapitalization or other change in the Company's capital structure that constitutes an equity restructuring within the meaning of FASB ASC 718, the Administrator will make appropriate adjustments to the maximum number of shares specified in Section 4(a) that may be delivered under the Plan and will also make appropriate adjustments to the number and kind of shares of stock or securities subject to Awards then outstanding or subsequently granted, any exercise prices relating to Awards and any other provision of Awards affected by such change.

(ii) Certain Other Adjustments. The Administrator may also make adjustments of the type described in Section 7(b)(i) above to take into account distributions to stockholders other than

those provided for in Section 7(a) and 7(b)(i), or any other event, if the Administrator determines that adjustments are appropriate to avoid distortion in the operation of the Plan, having due regard for the qualification of ISOs under Section 422 and the requirements of Section 409A, where applicable.

(iii) Continuing Application of Plan Terms. References in the Plan to shares of Stock will be construed to include any stock or securities resulting from an adjustment pursuant to this Section 7.

8. Legal Conditions on Delivery of Stock

The Company will not be obligated to deliver any shares of Stock pursuant to the Plan or to remove any restriction from shares of Stock previously delivered under the Plan until: (a) the Company is satisfied that all legal matters in connection with the issuance and delivery of such shares have been addressed and resolved; (b) if the outstanding Stock is at the time of delivery listed on any stock exchange or national market system, the shares to be delivered have been listed or authorized to be listed on such exchange or system upon official notice of issuance; and (c) all conditions of the Award have been satisfied or waived. The Company may require, as a condition to exercise of the Award, such representations or agreements as counsel for the Company may consider appropriate to avoid violation of the Securities Act or any applicable state or non-U.S. securities law. Any Stock required to be issued to Participants under the Plan will be evidenced in such manner as the Administrator may deem appropriate, including book-entry registration or delivery of stock certificates. In the event that the Administrator determines that Stock certificates will be issued to Participants under the Plan, the Administrator may require that certificates evidencing Stock issued under the Plan bear an appropriate legend reflecting any restriction on transfer applicable to such Stock, and the Company may hold the certificates pending lapse of the applicable restrictions.

9. Amendment and Termination

The Administrator may at any time or times amend the Plan or any outstanding Award for any purpose which may at the time be permitted by law, and may at any time terminate the Plan as to any future grants of Awards; provided, that except as otherwise expressly provided in the Plan the Administrator may not, without the Participant's consent, alter the terms of an Award so as to affect materially and adversely the Participant's rights under the Award, unless the Administrator expressly reserved the right to do so at the time the Award was granted. Any amendments to the Plan will be conditioned upon stockholder approval only to the extent, if any, such approval is required by law (including the Code and applicable stock exchange requirements), as determined by the Administrator.

10. Other Compensation Arrangements

The existence of the Plan or the grant of any Award will not in any way affect the Company's right to Award a person bonuses or other compensation in addition to Awards under the Plan.

11. Miscellaneous

(a) Waiver of Jury Trial. By accepting an Award under the Plan and to the extent permitted under applicable law, each Participant waives any right to a trial by jury in any action, proceeding or counterclaim concerning any rights under the Plan and any Award, or under any amendment, waiver, consent, instrument, document or other agreement delivered or which in the future may be delivered in connection therewith, and agrees that any such action, proceedings or counterclaim will be tried before a court and not before a jury. By accepting an Award under the Plan, each Participant certifies that no officer, representative, or attorney of the Company has represented, expressly or otherwise, that the Company would not, in the event of any action, proceeding or counterclaim, seek to enforce the foregoing waivers. Notwithstanding anything to the contrary in the Plan, nothing herein is to be construed as limiting the ability of the Company and a Participant to agree to submit disputes arising under the terms of the Plan or any Award made hereunder to binding arbitration or as limiting the ability of the Company to require any eligible individual to agree to submit such disputes to binding arbitration as a condition of receiving an Award hereunder.

(b) Limitation of Liability. Notwithstanding anything to the contrary in the Plan, neither the Company, nor any Affiliate, nor the Administrator, nor any person acting on behalf of the Company, any Affiliate, or the Administrator, will be liable to any Participant or to the estate or beneficiary of any Participant or to any other holder of an Award by reason of any acceleration of income, or any additional tax (including any interest and penalties), asserted by reason of the failure of an Award to satisfy the requirements of Section 422 or Section 409A or by reason of Section 4999 of the Code, or otherwise asserted with respect to the Award.

12. Establishment of Sub-Plans

The Administrator may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable blue sky, securities or tax laws of various jurisdictions. The Administrator will establish such sub-plans by adopting supplements to the Plan setting forth (a) such limitations on the Administrator's discretion under the Plan as it deems necessary or desirable and (b) such additional terms and conditions not otherwise inconsistent with the Plan as it deems necessary or desirable. All supplements so established will be deemed to be part of the Plan, but each supplement will apply only to Participants within the affected jurisdiction (as determined by the Administrator).

13. Governing Law

(a) Certain Requirements of Corporate Law. Awards will be granted and administered consistent with the requirements of applicable Delaware law relating to the issuance of stock and the consideration to be received therefor, and with the applicable requirements of the stock exchanges or other trading systems on which the Stock is listed or entered for trading, in each case as determined by the Administrator.

(b) Other Matters. Except as otherwise provided by the express terms of an Award agreement, under a sub-plan described in Section 12 or as provided in Section 13(a) above, the provisions of the Plan and of Awards under the Plan and all claims or disputes arising out of or based upon the Plan or any Award under the Plan or relating to the subject matter hereof or thereof will be governed by and construed in accordance with the domestic substantive laws of the State of Delaware without giving effect to any choice or conflict of laws provision or rule that would cause the application of the domestic substantive laws of any other jurisdiction.

(c) Jurisdiction. By accepting an Award, each Participant will be deemed to (a) have submitted irrevocably and unconditionally to the jurisdiction of the federal and state courts located within the geographic boundaries of the United States District Court for the Northern District of California for the purpose of any suit, action or other proceeding arising out of or based upon the Plan or any Award; (b) agree not to commence any suit, action or other proceeding arising out of or based upon the Plan or an Award, except in the federal and state courts located within the geographic boundaries of the United States District Court for the Northern District of California; and (c) waive, and agree not to assert, by way of motion as a defense or otherwise, in any such suit, action or proceeding, any claim that it is not subject personally to the jurisdiction of the above-named courts that its property is exempt or immune from attachment or execution, that the suit, action or proceeding is brought in an inconvenient forum, that the venue of the suit, action or proceeding is improper or that the Plan or an Award or the subject matter thereof may not be enforced in or by such court.

EXHIBIT A

Definition of Terms

The following terms, when used in the Plan, will have the meanings and be subject to the provisions set forth below:

"Administrator": The Compensation Committee, except that the Compensation Committee may, subject to applicable law, delegate (i) to one or more of its members (or one or more other members of the Board (including the full Board)) such of its duties, powers and responsibilities as it may determine; (ii) to one or more officers or Employees of the Company the power to grant Awards to the extent permitted by Section 157(c) of the Delaware General Corporation Law; and (iii) to such Employees or other persons as it determines such ministerial tasks as it deems appropriate. In the event of any delegation described in the preceding sentence, the term "Administrator" will include the person or persons so delegated to the extent of such delegation.

"Affiliate": Any corporation or other entity that stands in a relationship to the Company that would result in the Company and such corporation or other entity being treated as one employer under Section 414(b) and Section 414(c) of the Code.

"Award": Any or a combination of the following:

- **(i)** Stock Options.
- **(ii)** SARs.
- **(iii)** Restricted Stock.
- **(iv)** Unrestricted Stock.
- **(v)** Stock Units, including Restricted Stock Units.
- **(vi)** Performance Awards.
- **(vii)** Cash Awards.
- **(viii)** Awards (other than Awards described in (i) through (vii) above) that are convertible into or otherwise based on Stock.

"Board": The Board of Directors of the Company.

"Cash Award": An Award denominated in cash.

"Cause": In the case of any Participant who is party to an employment or severance-benefit agreement that contains a definition of "Cause," the definition set forth in such agreement will apply with respect to such Participant under the Plan. In the case of any other Participant, "Cause" will mean, as determined by the Administrator in its reasonable judgment, (i) a substantial failure of the Participant to perform the Participant's duties and responsibilities to the Company or subsidiaries or substantial negligence in the performance of such duties and responsibilities; (ii) the commission by the Participant of a felony or a crime involving moral turpitude; (iii) the commission by the Participant of theft, fraud, embezzlement, material breach of trust or any material act of dishonesty involving the Company or any of its subsidiaries; (iv) a significant violation by the Participant of the code of conduct of the Company or its subsidiaries of any material policy of the Company or its subsidiaries, or of any statutory or common law duty of loyalty to the Company or its subsidiaries; (v) material breach of any of the terms of the Plan or any Award made under the Plan, or of the terms of any other agreement between the Company or subsidiaries and the Participant; or (vi) other conduct by the Participant that could be expected to be harmful to the business, interests or reputation of the Company.

"Code": The U.S. Internal Revenue Code of 1986 as from time to time amended and in effect, or any successor statute as from time to time in effect.

"Company": Ultragenyx Pharmaceutical Inc., and except as utilized in the definition of Covered Transaction, any successor corporation.

"Compensation Committee": The Compensation Committee of the Board.

"Covered Transaction": The occurrence of any one of the following events:

- **(i)** a consolidation, merger, or similar transaction or series of related transactions in which the Company is not the surviving corporation or which results in the acquisition of all or substantially all of the Company's then outstanding Stock by a single person or entity or by a group of persons and/or entities acting in concert (a "**Transaction**"), excluding a Transaction which would result in the holders of the voting securities of the Company outstanding immediately prior to such merger or consolidation continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or any parent thereof) at least 50% of the combined voting power of the securities of the Company or such surviving entity or any parent thereof outstanding immediately after such merger or consolidation;
- **(ii)** a sale or transfer of all or substantially all the Company's assets, excluding a sale or transfer to an entity, at least 50% of the combined voting power of the voting securities of which is owned by stockholders of the Company in substantially the same proportions as their ownership of the Company immediately prior to such sale; or
- **(iii)** a dissolution or liquidation of the Company.

Where a Covered Transaction involves a tender offer that is reasonably expected to be followed by a merger described in clause (i) (as determined by the Administrator), the Covered Transaction will be deemed to have occurred upon consummation of the tender offer. Notwithstanding the foregoing, for each Award that constitutes deferred compensation under Section 409A, and to the extent required to avoid accelerated taxation and/or tax penalties under Section 409A, a Covered Transaction shall be deemed to have occurred under the Plan with respect to such Award only if a change in the ownership or effective control of the Company or a change in ownership of a substantial portion of the assets of the Company shall also be deemed to have occurred under Section 409A.

"Date of Adoption": March 24, 2025

"Employee": Any person who is employed by the Company or an Affiliate.

"Employment": A Participant's employment or other service relationship with the Company and its Affiliates, which may include service as a director, consultant or independent contractor. Employment will be deemed to continue, unless the Administrator expressly provides otherwise, so long as the Participant is employed by, or otherwise is providing services in a capacity described in Section 5 to the Company or an Affiliate. If a Participant's employment or other service relationship is with an Affiliate and that entity ceases to be an Affiliate, the Participant's Employment will be deemed to have terminated when the entity ceases to be an Affiliate unless the Participant transfers Employment to the Company or its remaining Affiliates. Notwithstanding the foregoing and the definition of "Affiliate" above, in construing the provisions of any Award relating to the payment of "nonqualified deferred compensation" (subject to Section 409A) upon a termination or cessation of Employment, references to termination or cessation of employment, separation from service, retirement or similar or correlative terms will be construed to require a "separation from service" (as that term is defined in Section 1.409A-1(h) of the Treasury Regulations) from the Company and from all other corporations and trades or businesses, if any, that would be treated as a single "service recipient" with the Company under Section 1.409A-1(h)(3) of the Treasury Regulations. The Company may, but need not, elect in writing, subject to the applicable limitations under Section 409A, any of the special elective rules prescribed in Section 1.409A-1(h) of the Treasury Regulations for purposes of determining whether a "separation from service" has occurred. Any such written election will be deemed a part of the Plan.

"Fair Market Value":

(a) If the Stock is readily traded on an established national exchange or trading system (including the Nasdaq Global Market), the closing price of the Stock as reported by the principal exchange on which such Stock is traded; provided, however, that if such day is not a trading day, Fair Market Value will mean the reported closing price of the Stock for the immediately preceding day that is a trading day.

(b) If the Stock is not traded on an established national exchange or trading system, the average of the bid and ask prices for such Stock where the bid and ask prices are quoted.

(c) If the Stock cannot be valued pursuant to clauses (a) or (b), the value as determined in good faith by the Board in its sole discretion consistent with the rules of Section 422 and Section 409A to the extent applicable.

"ISO": A Stock Option intended to be an "incentive stock option" within the meaning of Section 422. Each Stock Option granted pursuant to the Plan will be treated as providing by its terms that it is to be an NSO unless, as of the date of grant, it is expressly designated as an ISO.

"NSO": A Stock Option that is not intended to be an "incentive stock option" within the meaning of Section 422.

"Participant": A person who is granted an Award under the Plan.

"Original Effective Date": June 7, 2023.

"Performance Award": An Award subject to Performance Criteria.

"Performance Criteria": Specified criteria, other than the mere continuation of Employment or the mere passage of time, the satisfaction of which is a condition for the grant, exercisability, vesting or full enjoyment of an Award. Performance Criteria will include but not be limited to any objectively determinable measure of performance relating to any, or any combination, of the following (measured either absolutely or by reference to an index or indices and determined either on a consolidated basis or, as the context permits, on a divisional, subsidiary, line of business, project or geographical basis or in combinations thereof): sales; revenues; assets; expenses; earnings from operations; earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization, incentives, service fees or extraordinary or special items, whether or not on a continuing operations or an aggregate or per share basis; net income or net income per common share (basic or diluted); return on equity, investment, capital or assets; one or more operating ratios; borrowing levels, leverage ratios or credit rating; market share; capital expenditures; cash flow, free cash flow, cash flow return on investment, or net cash provided by operations; stock price, dividends or total stockholder return; development of new technologies or products; sales of particular products or services; economic value created or added; operating margin or profit margin; customer acquisition or retention; raising or refinancing of capital; successful hiring of key individuals; resolution of significant litigation; acquisitions and divestitures (in whole or in part); joint ventures and strategic alliances; spin-offs, split-ups and the like; reorganizations; recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; or strategic business criteria, consisting of one or more objectives based on the following goals: meeting specified market penetration or value added, product development or introduction (including, without limitation, any clinical trial accomplishments, regulatory or other filings or approvals, or other product development milestones), geographic business expansion, cost targets, cost reductions or savings, customer satisfaction, operating efficiency, acquisition or retention, employee satisfaction, information technology, corporate development (including, without limitation, licenses, innovation, research or establishment of third party collaborations), manufacturing or process development, legal compliance or risk reduction, patent application or issuance goals, or goals relating to acquisitions or divestitures (in whole or in part), joint ventures or strategic alliances. Performance Criteria and any targets with respect thereto determined by the Administrator need not be based upon an increase, a positive or improved result or avoidance of loss.

"Plan": The Ultragenyx Pharmaceutical Inc. 2023 Incentive Plan as amended and restated effective as of the Effective Date, and as from time to time amended and in effect.

"Prior Plans": The Ultragenyx Pharmaceutical Inc. 2011 Incentive Plan and the Ultragenyx Pharmaceutical Inc. 2014 Incentive Plan, in each case as amended from time to time.

"Restricted Stock": Stock subject to restrictions requiring that it be redelivered or offered for sale to the Company if specified conditions are not satisfied.

"Restricted Stock Unit": A Stock Unit that is, or as to which the delivery of Stock or cash in lieu of Stock is, subject to the satisfaction of specified performance or other vesting conditions.

"SAR": A right entitling the holder upon exercise to receive an amount (payable in cash or in shares of Stock of equivalent value) equal to the excess of the Fair Market Value of the shares of Stock subject to the right over the base value from which appreciation under the SAR is to be measured.

"Section 409A": Section 409A of the Code.

"Section 422": Section 422 of the Code.

"Securities Act": The U.S. Securities Act of 1933, as amended.

"Stock": Common stock of the Company, par value $0.001 per share.

"Stock Option": An option entitling the holder to acquire shares of Stock upon payment of the exercise price.

"Stock Unit": An unfunded and unsecured promise, denominated in shares of Stock, to deliver Stock or cash measured by the value of Stock in the future.

"Unrestricted Stock": Stock not subject to any restrictions under the terms of the Award.

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